U.S. DEPARTMENT OF COMMERCE
Patent and Trademark Office

SEARCH REQUEST FORM

6-18

Requestor's Name: GARY L. KUNZ

Serial Number: 07/652,978

Date: 6/4/96 Phone: X.4623 Art Unit: 1211

Search Topic:

Please write a detailed statement of search topic. Describe specifically as possible the subject matter to be searched. Define any terms that may have a special meaning. Give examples or relevant citations, authors keywords, etc., if known. For sequences, please attach a copy of the sequence. You may include a copy of the broadest and/or most relevant claim(s).

PLS. SEARCH ATTACHED claims 51-67 in CAS, Bellstein, & MARPAT

THX.

Gary K.

L21= guanine

6-8-96 **STAFF USE ONLY**

Date completed:

Searcher: JOHN DANTZMAN

Terminal time: 2

Elapsed time:

CPU time:

Total time:

Number of Searches: S

Number of Databases: S

Search Site

- ___ STIC
- ✓ CM-1
- ___ Pre-S

Type of Search

- ___ N.A. Sequence
- ___ A.A. Sequence
- ✓ Structure
- ___ Bibliographic

Vendors

- ___ IG Suite
- ✓ STN
- ___ Dialog
- ___ APS
- ___ Geninfo
- ___ SDC
- ___ DARC/Questel
- ___ Other

Reg Map Beilst.

PTO-1590 (9-90)

★ U.S. GPO: 1995-398-798/22489

USCOMM-DC 90-3952

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=> D HIS

     (FILE 'REGISTRY' ENTERED AT 08:01:10 ON 08 JUN 96)
                DEL HIS Y
L1                STR
L2              1 S L1
L3              1 S L1 FUL
L4                STR L1
L5              8 S L4
L6                STR L4
L7              3 S L6
L8                STR L6
L9                STR L8
L10             1 S L6 AND L9
L11               STR L6
L12               STR L11
L13             1 S L11 AND L12
L14             3 S L11
L15            94 S L11 FUL
L16            48 S L12 SSS FUL SUB=L15
L17             8 S L16 AND F/ELS
L18               STR L12

     FILE 'CAPLUS' ENTERED AT 08:32:10 ON 08 JUN 96

     FILE 'REGISTRY' ENTERED AT 08:32:23 ON 08 JUN 96
L19            20 S L18 SSS FUL SUB=L16

     FILE 'CAPLUS' ENTERED AT 08:33:14 ON 08 JUN 96

     FILE 'REGISTRY' ENTERED AT 08:33:34 ON 08 JUN 96
L20            27 S L19 OR L17
L21             5 S L20 AND NCNC2-NCNC3/ES
L22             8 S L17 NOT L21
L23            15 S L19 NOT L21

     FILE 'CAPLUS' ENTERED AT 08:35:42 ON 08 JUN 96
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L25             1 S L21
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=> D QUE L17
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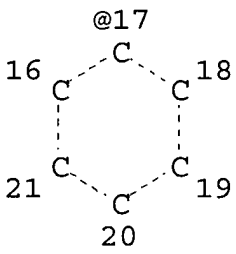

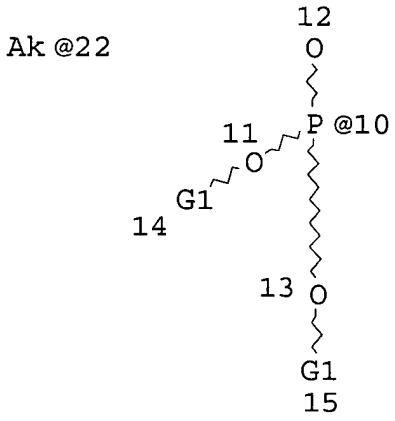

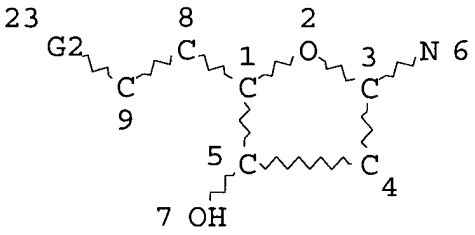

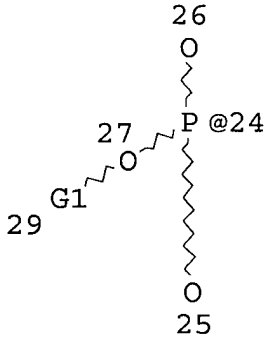

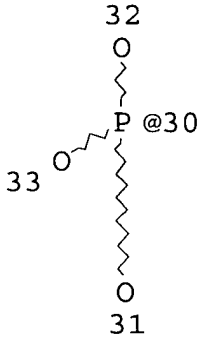

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CONNECT IS E1 RC AT 31
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CONNECT IS E1 RC AT 33
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE
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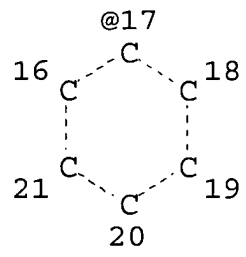

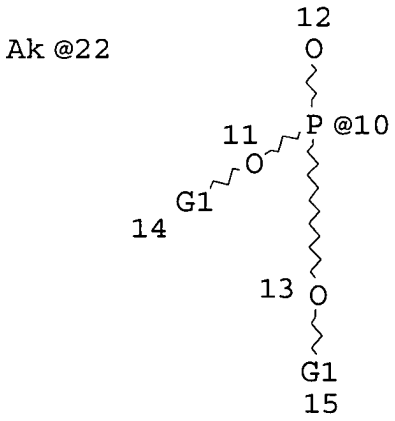

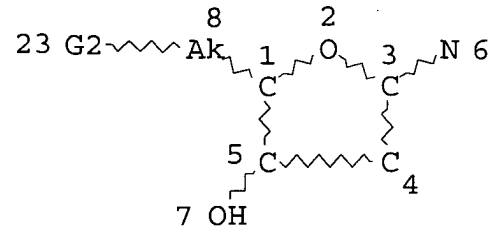

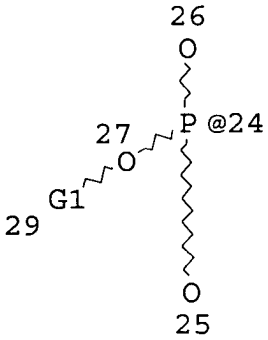

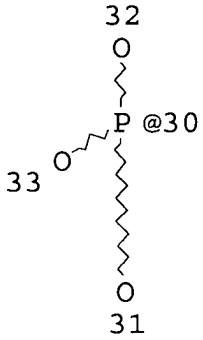

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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 31

STEREO ATTRIBUTES: NONE
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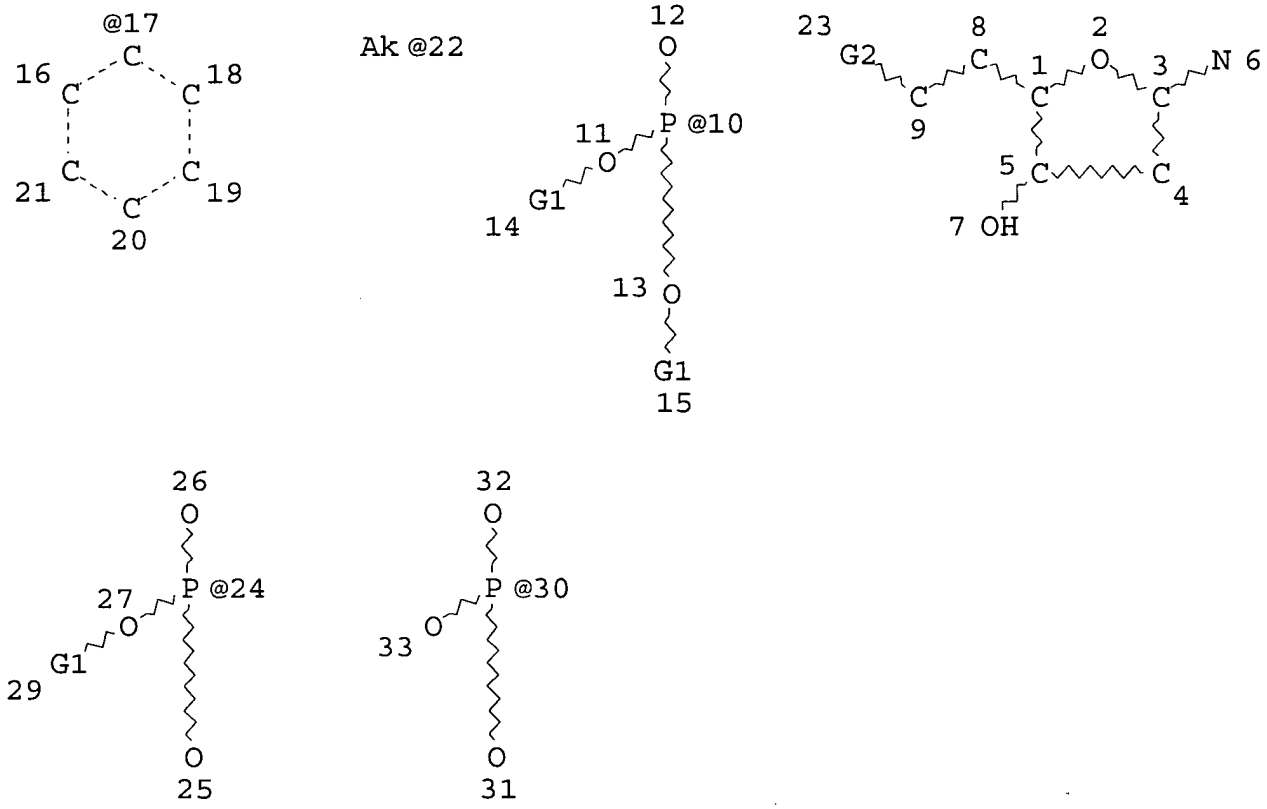
L16 48 SEA FILE=REGISTRY SUB=L15 SSS FUL L12
L17 8 SEA FILE=REGISTRY L16 AND F/ELS

=> D QUE L19
L11 STR



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CONNECT IS E1 RC AT 25
CONNECT IS E1 RC AT 26
CONNECT IS E1 RC AT 31
CONNECT IS E1 RC AT 32
CONNECT IS E1 RC AT 33
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 32

STEREO ATTRIBUTES: NONE
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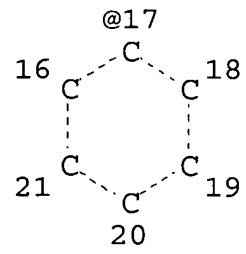

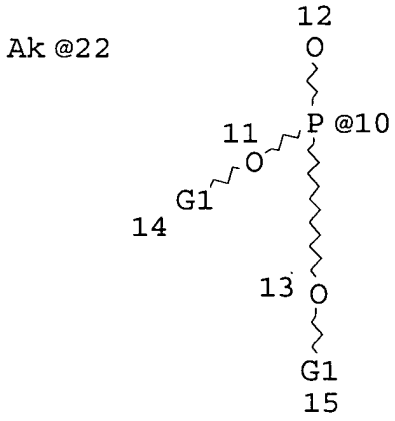

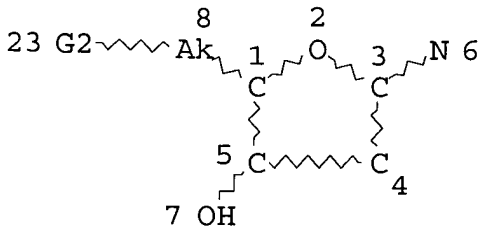

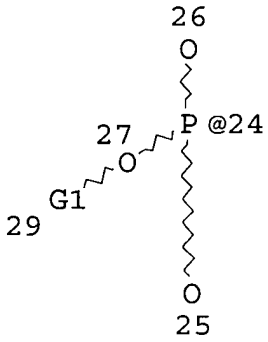

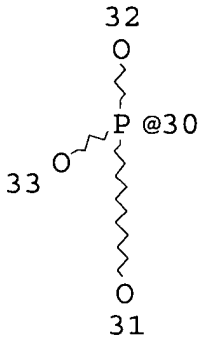

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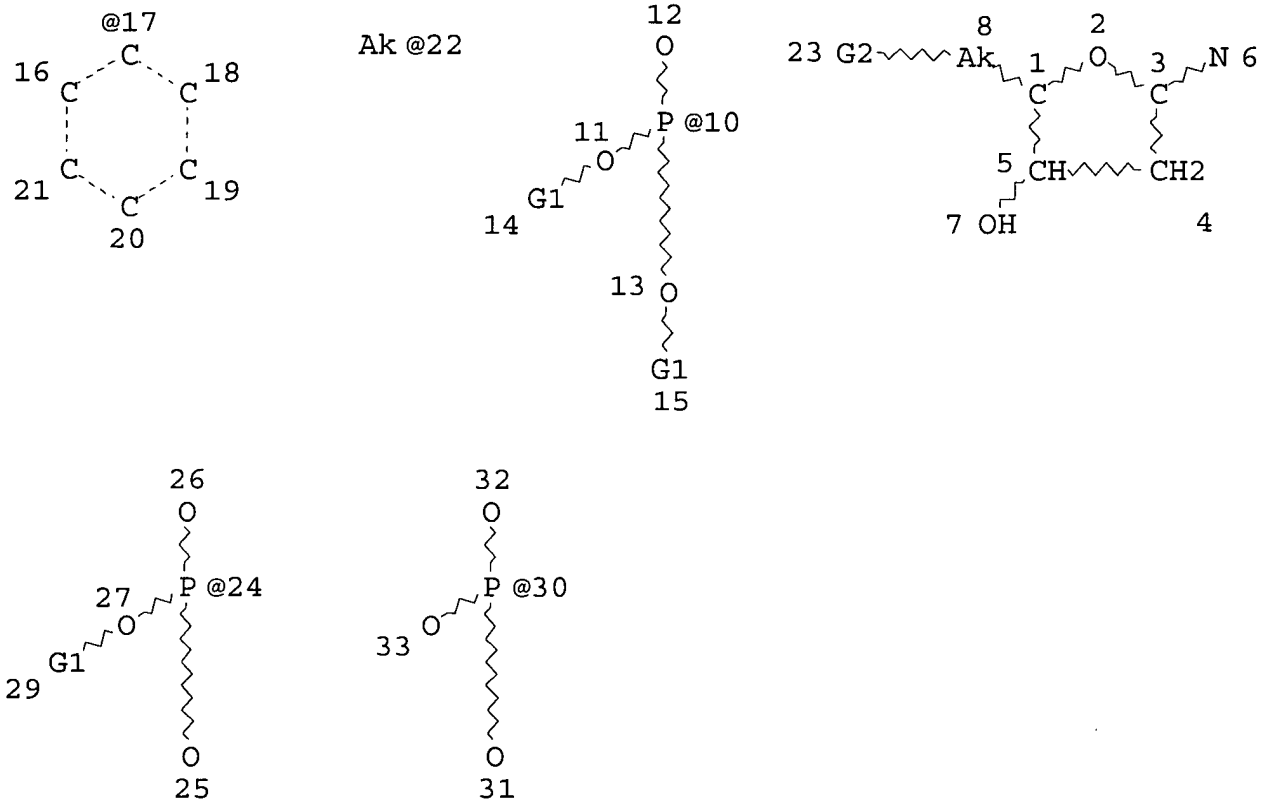
L16 48 SEA FILE=REGISTRY SUB=L15 SSS FUL L12
L18 STR



VAR G1=17/22
VAR G2=10/24/30
NODE ATTRIBUTES:
NSPEC IS R AT 6
CONNECT IS E2 RC AT 8
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CONNECT IS E1 RC AT 25
CONNECT IS E1 RC AT 26
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DEFAULT MLEVEL IS ATOM
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RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 31

STEREO ATTRIBUTES: NONE
L19 20 SEA FILE=REGISTRY SUB=L16 SSS FUL L18

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=> D HIS

     (FILE 'REGISTRY' ENTERED AT 08:01:10 ON 08 JUN 96)
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L1              STR
L2            1 S L1
L3            1 S L1 FUL
L4              STR L1
L5            8 S L4
L6              STR L4
L7            3 S L6
L8              STR L6
L9              STR L8
L10           1 S L6 AND L9
L11             STR L6
L12             STR L11
L13           1 S L11 AND L12
L14           3 S L11
L15          94 S L11 FUL
L16          48 S L12 SSS FUL SUB=L15
L17           8 S L16 AND F/ELS
L18             STR L12

     FILE 'CAPLUS' ENTERED AT 08:32:10 ON 08 JUN 96

     FILE 'REGISTRY' ENTERED AT 08:32:23 ON 08 JUN 96
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     FILE 'CAPLUS' ENTERED AT 08:33:14 ON 08 JUN 96

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L21           5 S L20 AND NCNC2-NCNC3/ES
L22           8 S L17 NOT L21
L23          15 S L19 NOT L21

     FILE 'CAPLUS' ENTERED AT 08:35:42 ON 08 JUN 96
L24           2 S L17
L25           1 S L21
L26          11 S L19
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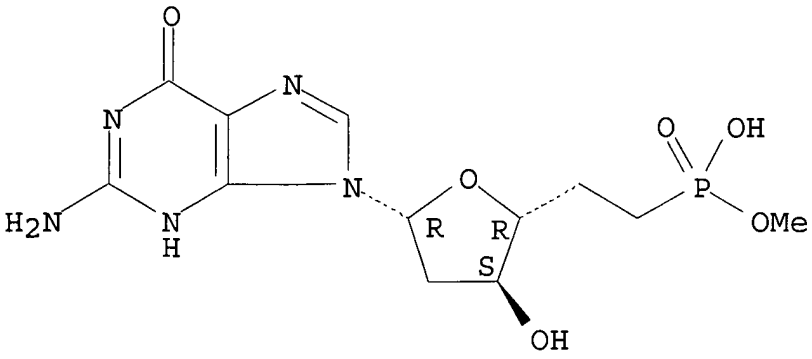
=> D L25 BIB ABS HITSTR

L25 ANSWER 1 OF 1 CAPLUS COPYRIGHT 1996 ACS
AN 1993:7326 CAPLUS
DN 118:7326
TI Methylenephosphonate nucleoside analogs and oligonucleotide analogs made therefrom
IN Buhr, Chris; Matteucci, Mark; Bischofberger, Norbert W.; Froehler, Brian
PA Gilead Sciences, Inc., USA
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
PI WO 9213869 A1 920820
DS W: AU, CA, FI, JP, KR, NO, RU
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE
AI WO 92-US1020 920207
PRAI US 91-652978 910208
DT Patent
LA English
OS MARPAT 118:7326
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Nucleoside phosphonates I [B = purine or pyrimidine nucleic acid base; R, R1 = (un)substituted OH, NH2, SH; R2 = H, allyloxy, allylthio, MeO, MeS, F; R3 = H, OH, F, OCH2Ph, OSiMe2CMe3, OCPh(C6H4OMe-4)2, OCPh2C6H4OMe-4; R2R3 = O, bond; X = O, S] were prepd. as intermediates for oligonucleotide analogs II (R4, R5 = H, protective group; n = 1-30). Thus, 3'-O-tert-butyldimethylsilyl-N2-isobutyryl-2'-deoxyguanosine was prepd. from 2'-deoxyguanosine in 3 steps and was treated with Ph3P:CHP(O)(OPh)2 followed by hydrogenation to give the phosphonate III.
IT **144822-53-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and ester hydrolysis of)
RN 144822-53-7 CAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-[2,5,6-trideoxy-6-(hydroxymethoxyphosphinyl)-.beta.-D-erythro-hexofuranosyl]-, monosodium salt (9CI) (CA INDEX NAME)

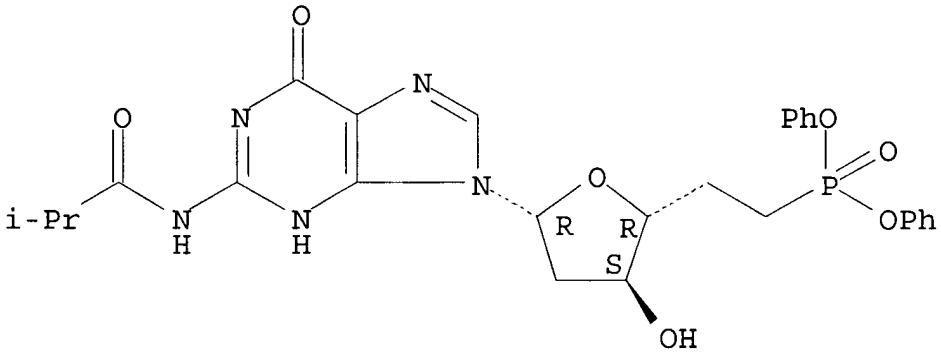
Absolute stereochemistry.



● Na

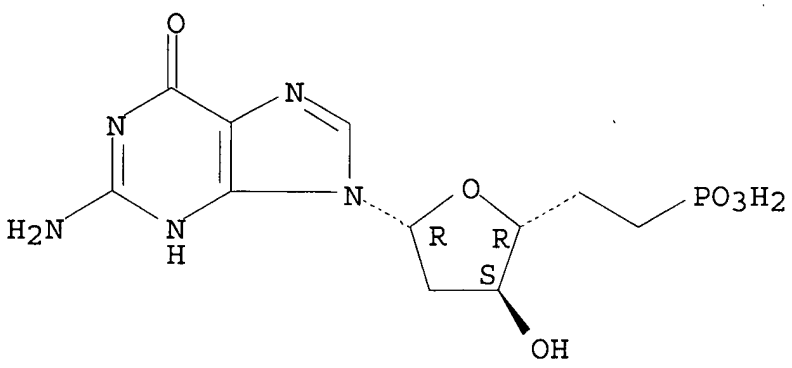
IT **144822-47-9P 144822-54-8P 144822-56-0P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 144822-47-9 CAPLUS
CN Propanamide, N-[6,9-dihydro-6-oxo-9-[2,5,6-trideoxy-6-(diphenoxyphosphinyl)-.beta.-D-erythro-hexofuranosyl]-1H-purin-2-yl]-2-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 144822-54-8 CAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-(2,5,6-trideoxy-6-phosphono-.beta.-D-erythro-hexofuranosyl)-, disodium salt (9CI) (CA INDEX NAME)

Absolute stereochemistry.



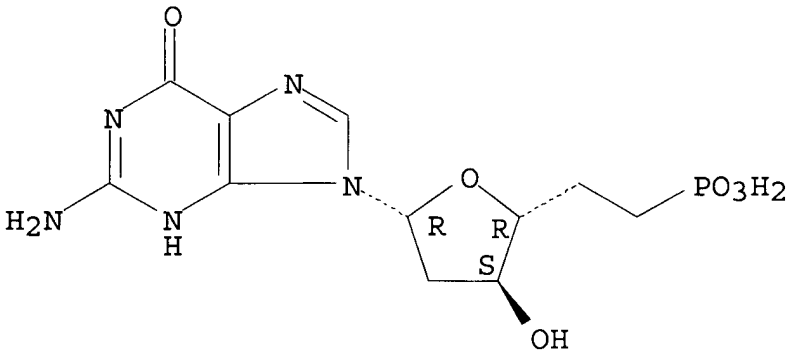
● 2 Na

RN 144822-56-0 CAPLUS
CN 6H-Purin-6-one, 2-amino-1,9-dihydro-9-(2,5,6-trideoxy-6-phosphono-.beta.-D-erythro-hexofuranosyl)-, monosodium salt, compd. with N,N-diethylethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

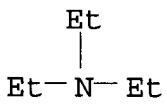
CRN 144822-55-9
CMF C11 H16 N5 O6 P
CDES 5:B-D-ERYTHRO

Absolute stereochemistry.



CM 2

CRN 121-44-8
CMF C6 H15 N



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=> D HIS

     (FILE 'REGISTRY' ENTERED AT 08:01:10 ON 08 JUN 96)
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L1              STR
L2            1 S L1
L3            1 S L1 FUL
L4              STR L1
L5            8 S L4
L6              STR L4
L7            3 S L6
L8              STR L6
L9              STR L8
L10           1 S L6 AND L9
L11             STR L6
L12             STR L11
L13           1 S L11 AND L12
L14           3 S L11
L15          94 S L11 FUL
L16          48 S L12 SSS FUL SUB=L15
L17           8 S L16 AND F/ELS
L18             STR L12

     FILE 'CAPLUS' ENTERED AT 08:32:10 ON 08 JUN 96

     FILE 'REGISTRY' ENTERED AT 08:32:23 ON 08 JUN 96
L19          20 S L18 SSS FUL SUB=L16

     FILE 'CAPLUS' ENTERED AT 08:33:14 ON 08 JUN 96

     FILE 'REGISTRY' ENTERED AT 08:33:34 ON 08 JUN 96
L20          27 S L19 OR L17
L21           5 S L20 AND NCNC2-NCNC3/ES
L22           8 S L17 NOT L21
L23          15 S L19 NOT L21

     FILE 'CAPLUS' ENTERED AT 08:35:42 ON 08 JUN 96
L24           2 S L17
L25           1 S L21
L26          11 S L19
L27           1 S L24 NOT L25
L28          10 S L26 NOT L25

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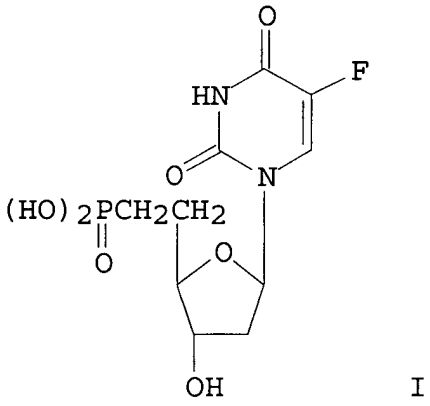
=> D BIB ABS HITSTR L27

L27 ANSWER 1 OF 1 CAPLUS COPYRIGHT 1996 ACS
AN 1979:97373 CAPLUS
DN 90:97373
TI Phosphonate analog of 2'-deoxy-5-fluorouridylic acid
AU Montgomery, John A.; Thomas, H. Jeanette
CS Sch. Med., Tufts Univ., Boston, Mass., USA
SO J. Med. Chem. (1979), 22(1), 109-11
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI

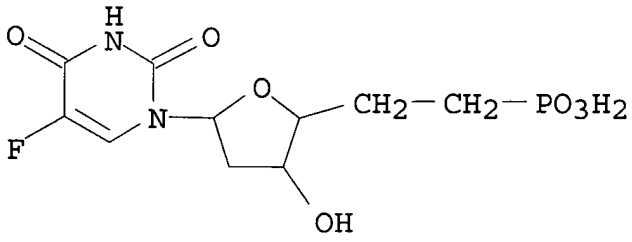


I

AB Ba 1-(2',5',6'-trideoxy-.beta.-D-ribohexofuranosyl)-5-fluorouracil-6'-phosphonate (I Ba) [**69124-08-9**] was prepd. by the oxidn. of 3'-O-acetyl-2'-deoxy-5-fluorouridine [2059-38-3] to the aldehyde, reaction of the aldehyde with diphenyl(triphenylphosphoranylidene)methylphosphonate [22400-41-5], to give the olefin, and redn. of the olefin to a satd. compd. followed by treatment with 3N NaOH. I inhibited thymidylate synthetase [9031-61-2] from Lactobacillus casei, Escherichia coli and Coliphage T2, and was cytotoxic to H. Ep-2 cells in culture.

IT **69124-08-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of and thymidylate synthetase inhibition by)

RN 69124-08-9 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-fluoro-1-(2,5,6-trideoxy-6-phosphono-.beta.-D-erythro-hexofuranosyl)-, barium salt (1:1) (9CI) (CA INDEX NAME)



● 3/2 Ba

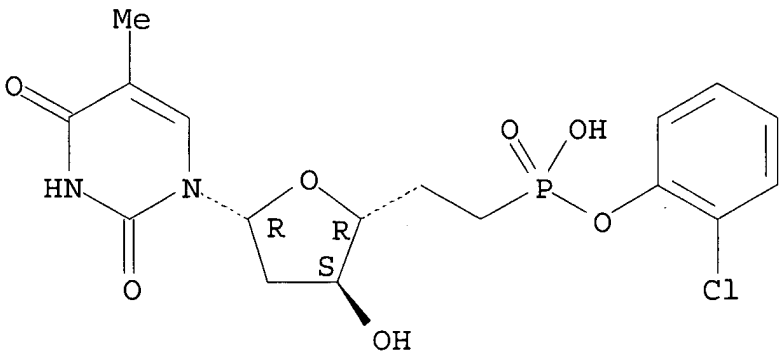
=> D BIB ABS HITSTR

L28 ANSWER 1 OF 10 CAPLUS COPYRIGHT 1996 ACS
AN 1995:505367 CAPLUS
DN 123:83926
TI Synthesis and some conformational features of the 5'-deoxy-5'-methylphosphonate linked dimer, 5'-deoxy-5'-C-(phosphonomethyl)thymidin-3'-yl (thymidin-5'-yl)methylphosphonate [p(CH2)Tp(CH2)T]
AU Szabo, Tomas; Stawinski, Jacek
CS Dep. Org. Chem., Stockholm Univ., Stockholm, S-106 91, Swed.
SO Tetrahedron (1995), 51(14), 4145-60
CODEN: TETRAB; ISSN: 0040-4020
DT Journal
LA English
AB Efficient synthesis of the 5'-deoxy-5'-methylphosphonate linked thymidine dimer [p(CH2)Tp(CH2)T] was developed via the 5'-deoxy-5'-C-(phosphomomethyl)-3'-silylated thymidine as a key intermediate. Conformational anal. of the sugar parts of the dimer showed that the deoxyribose residues exist in soln. mainly in the S-type conformation but with a predominant contribution of antiperiplanar rotamers around the C4'-C5' bonds in both sugar units.
IT **165131-56-6P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(synthesis and conformation of deoxymethylphosphonate linked thymidine dimer)
RN 165131-56-6 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[6-[(2-chlorophenoxy)hydroxyphosphinyl]-2,5,6-trideoxy-.beta.-D-erythro-hexofuranosyl]-5-methyl-, compd. with pyridine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 165131-55-5
CMF C17 H20 Cl N2 O7 P
CDES 5:B-D-ERYTHRO

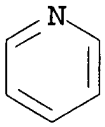
Absolute stereochemistry.



CM 2

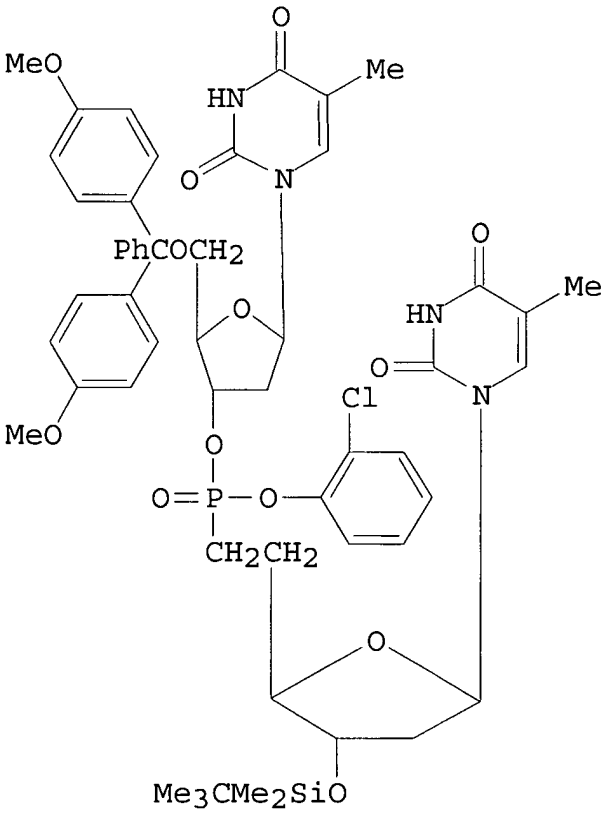
CRN 110-86-1

CMF C5 H5 N



=> D BIB ABS HITSTR 2

L28 ANSWER 2 OF 10 CAPLUS COPYRIGHT 1996 ACS
AN 1993:581133 CAPLUS
DN 119:181133
TI Synthesis of 5'-deoxy-5'-methylphosphonate linked thymidine oligonucleotides
AU Boehringer, Markus P.; Graff, Darla; Caruthers, Marvin H.
CS Dep. Chem. Biochem., Univ. Colorado, Boulder, CO, 80309-0215, USA
SO Tetrahedron Lett. (1993), 34(17), 2723-6
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
GI

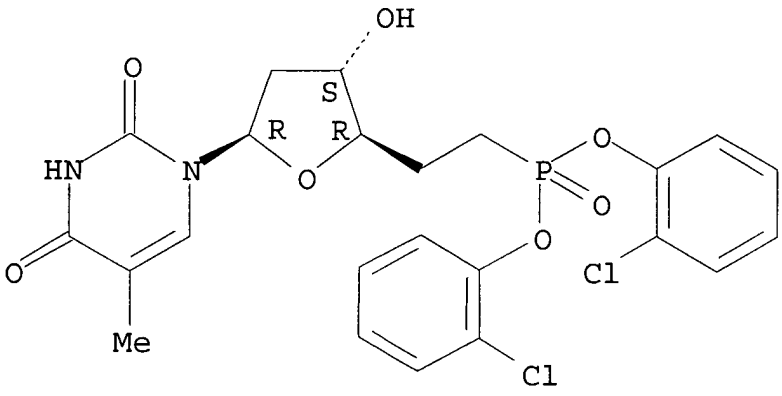


I

AB A 5'-deoxy-5'-methylphosphonate linked thymidine dinucleotide I was synthesized and its 3'-phosphoramidite used to synthesize the title oligonucleotides dT6(T5'mpT)T6 and dT(T5'mpT)6T (5'mp = 5'-deoxy-5'-methylphosphonate) along with dT14.

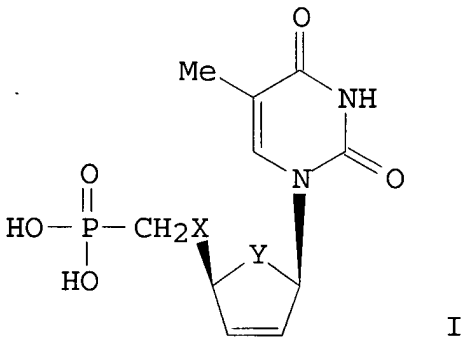
IT **149741-61-7P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and silylation of)
RN 149741-61-7 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 1-[6-[bis(2-chlorophenoxy)phosphinyl]-2,5,6-trideoxy-.beta.-D-erythro-hexofuranosyl]-5-methyl- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> D BIB ABS HITSTR 3

L28 ANSWER 3 OF 10 CAPLUS COPYRIGHT 1996 ACS
AN 1993:496051 CAPLUS
DN 119:96051
TI Synthesis and HIV activity of phosphonate isosteres of d4T monophosphate
AU Kim, Choung Un; Bronson, Joanne J.; Ferrara, Louis M.; Martin, John C.
CS Pharm. Res. Inst., Bristol-Myers Squibb Co., Wallingford, CT, 06492-7660, USA
SO Bioorg. Med. Chem. Lett. (1992), 2(5), 367-70
CODEN: BMCLE8; ISSN: 0960-894X
DT Journal
LA English
GI



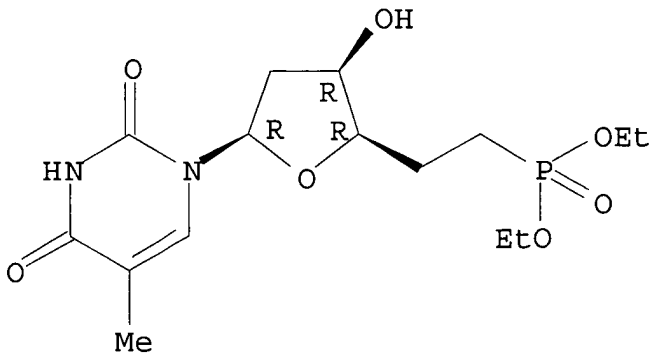
I

AB Nucleotide phosphonates, e.g. I (X = O, Y = CH2; X = CH2, Y = O), were prepd. and tested for their anti-HIV activity.

IT **124685-23-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and mesylation of)

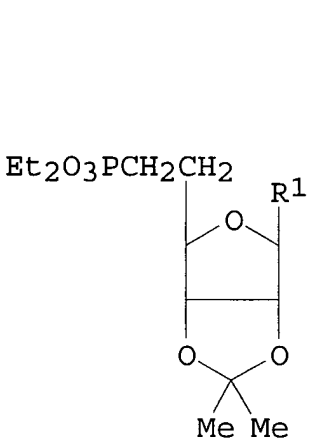
RN 124685-23-0 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-methyl-1-[2,5,6-trideoxy-6-(diethoxyphosphinyl)-.beta.-D-threo-hexofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

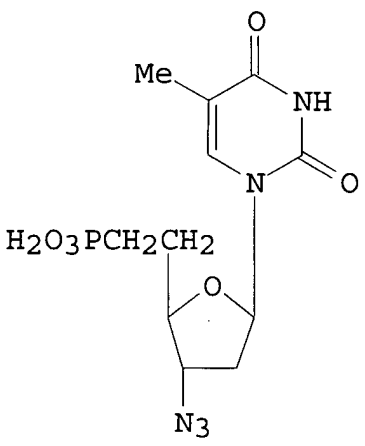


=> D BIB ABS HITSTR 4

L28 ANSWER 4 OF 10 CAPLUS COPYRIGHT 1996 ACS
AN 1992:236116 CAPLUS
DN 116:236116
TI New synthesis of sugar, nucleoside and .alpha.-amino acid phosphonates
AU Barton, Derek H. R.; Gero, Stephane D.; Quiclet-Sire, Beatrice; Samadi, Mohammad
CS Dep. Chem., Texas A and M Univ., College Station, TX, 77843, USA
SO Tetrahedron (1992), 48(9), 1627-36
CODEN: TETRAB; ISSN: 0040-4020
DT Journal
LA English
OS CASREACT 116:236116
GI



II



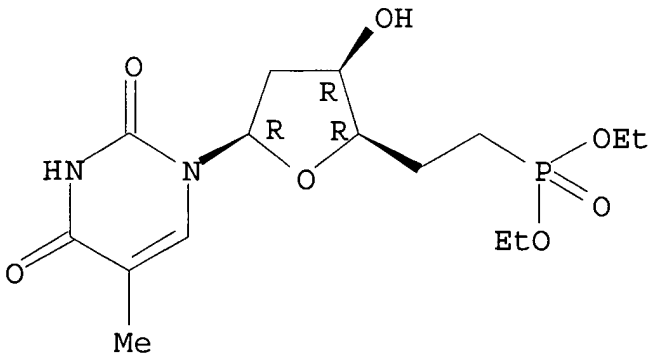
III

AB Photolysis of N-hydroxy-2-thiopyridone esters derived from uronic acids or .alpha.-amino acids in presence of vinyl phosphonate affords the corresponding phosphonate derivs. Thus, in situ esterification of protected amino acids Boc-X-OCH2Ph (Boc = Me3CO2C; X = Asp, Glu) with N-hydroxy-2-thiopyridone followed by radical addn. with H2C:CHPO3Et2 gave phosphonates Boc-L-NHCH(CO2CH2Ph)(CH2)nCHRPO3Et2 (I; n = 2, 3; R = 2-pyridylthio). Removal of the thiopyridyl groups in I with Bu3SnH gave phosphonic acid analogs I (R = H). Sugar and nucleoside phosphonates II (R1 = OMe, protected adenine, uracil) were prepd. similarly. A convenient route for the synthesis of III, the isostere of AZT-5' monophosphate, is described.

IT **124685-23-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and mesylation of)

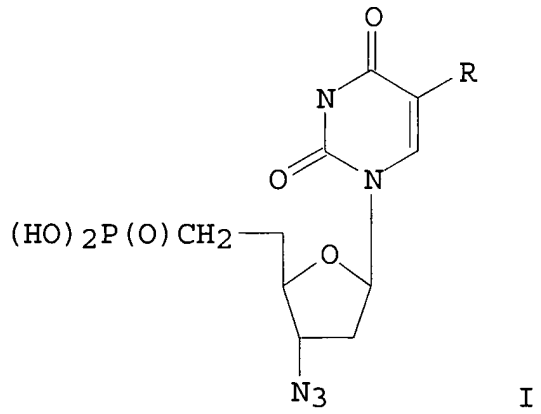
RN 124685-23-0 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-methyl-1-[2,5,6-trideoxy-6-(diethoxyphosphinyl)-.beta.-D-threo-hexofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

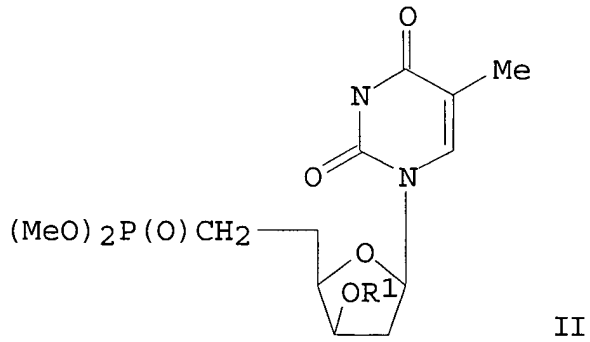

OH
O
R
R
R
HN
N
O
OEt
P
O
EtO
O
Me

=> D BIB ABS HITSTR 5

L28 ANSWER 5 OF 10 CAPLUS COPYRIGHT 1996 ACS
AN 1991:122988 CAPLUS
DN 114:122988
TI Preparation of virucidal 3'-deoxy-3'-azidonucleoside 5'-phosphonic acids
IN Miyasaka, Sada; Tanaka, Hiromichi
PA Mitsubishi Kasei Corp., Japan
SO Jpn. Kokai Tokkyo Koho, 3 pp.
CODEN: JKXXAF
PI JP 02262588 A2 901025 Heisei
AI JP 89-84298 890403
DT Patent
LA Japanese
OS MARPAT 114:122988
GI



I

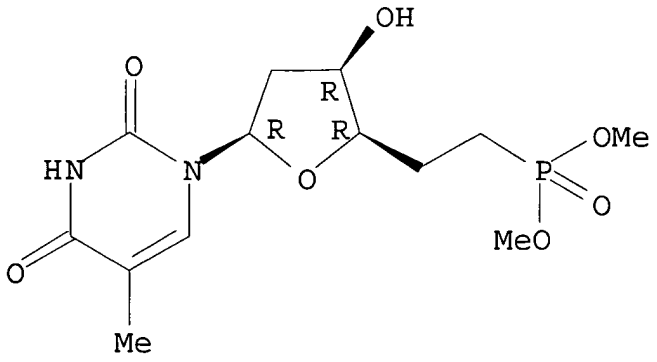


II

AB Title compds. I (R = H, C1-4 alkyl) and their pharmacol. acceptable salts, useful as virucides for retrovirus (e.g. human immunodeficiency virus) (no data), are prepd. Treatment of 209 mg thymidine analog II (R1 = H) (prepn. given) with mesyl chloride and p-dimethylaminopyridine in pyridine at 0.degree. for 7 h gave 345 mg II (R1 = mesyl), which was treated with NaN3 in DMF at 80.degree. for 17 h to afford 165 mg I (R = Me) di-Me ester. NaBr was treated with Me3SiCl in DMF at 40.degree. for 5 min, treated with 110 mg I (R = Me) di-Me ester at 40.degree. for 5 h, and the product was chromatographed on Dowex 50 .times. 8 (Na-type) to give 107 mg I (R = Me) di-Na salt.

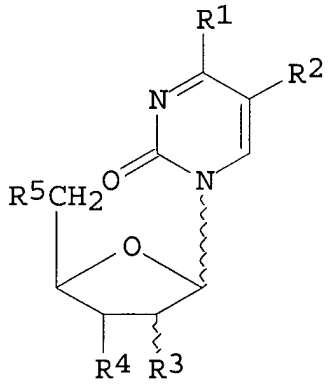
IT **124685-22-9P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and mesylation of)
RN 124685-22-9 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-methyl-1-[2,5,6-trideoxy-6-(dimethoxyphosphinyl)-.beta.-D-threo-hexofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

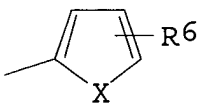

OH
O
R
R
R
OMe
HN
N
O
P
O
MeO
O
Me

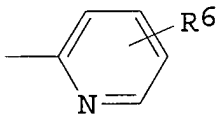
=> D BIB ABS HITSTR 6

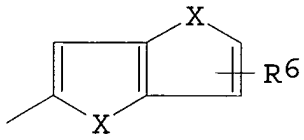
L28 ANSWER 6 OF 10 CAPLUS COPYRIGHT 1996 ACS
AN 1990:235778 CAPLUS
DN 112:235778
TI Preparation of pyrimidine nucleosides as virucides and their intermediates
IN Johansson, K. Nils Gunnar; Malmberg, Hans C. G.; Noreen, Rolf; Sahlberg, S. Christer; Sohn, Daniel D.; Gronowitz, Salo
PA Medivir AB, Swed.
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
PI WO 8912061 A1 891214
DS W: AU, DK, FI, HU, JP, KR, NO, US
AI WO 89-SE322 890607
PRAI SE 88-2173 880610
DT Patent
LA English
OS MARPAT 112:235778
GI



I

Q= 

Q1= 

Q2= 

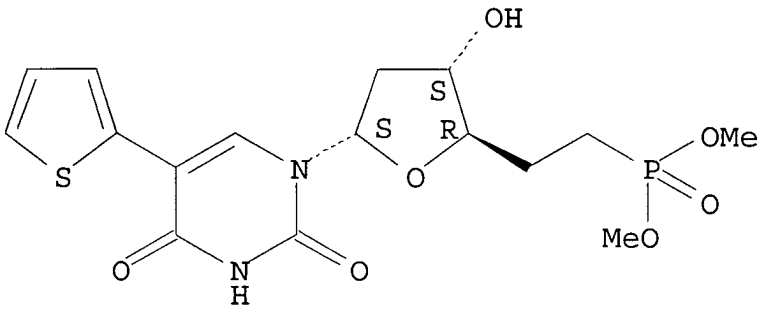
AB The title compds. [I; R1 = OH, NH2; R2 = (hetero)aryl, e.g. Q-Q2; X = O, S, Se, (un)substituted NH; R3 = H, OH, F, OMe; R4 = H, F, OH or its ether or ester residue, OMe, cyano, C.tplbond.CH, N3; R5 = OH or its ether or ester residue, (CH2)nP(O)(OM)2, (CH2)nP(O)(OM)CH2P(O)(OM)2; R6 = H, straight or branched C1-10 alkyl, halo, etc.; M = H, a pharmaceutically acceptable counterion; n = 0, 1], useful for treatment of infections by viruses requiring reverse transcriptase for replication, e.g. human immunodeficiency virus (HIV) and hepatitis B virus, were prepd. Thus, silylation of 5-(2-thienyl)uracil (II) with hexamethyldisilazane in the presence of Me3SiCl and (NH4)2SO4 under reflux gave bis-trimethylsilylated II which was stirred overnight with 2-deoxy-3,5-di-O-p-toluoyl-D-ribofuranosyl chloride in ClCH2CH2Cl in the presence of mol. sieve 4A. The product was treated with MeONa in MeOH to give .alpha.- and .beta.-I (R1 = R4 = R5 = OH, R2 = 2-thienyl, R3 = H). .alpha.-I in

vitro showed IC50 of 0.05-10 .mu.M against HIV in H9 cells. Analogously prepd. and tested were addnl. 26 I. Cellular toxicity of I on H9 and F500 cells and inhibition of enzymes (e.g. HIV reverse transcriptase, hepatitis B virus DNA polymerase, and herpes simplex virus type 2 DNA polymerase) by I were also given.

IT **127235-90-9P 127235-91-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and reaction of, in prepn. of pyrimidine nucleoside virucide)

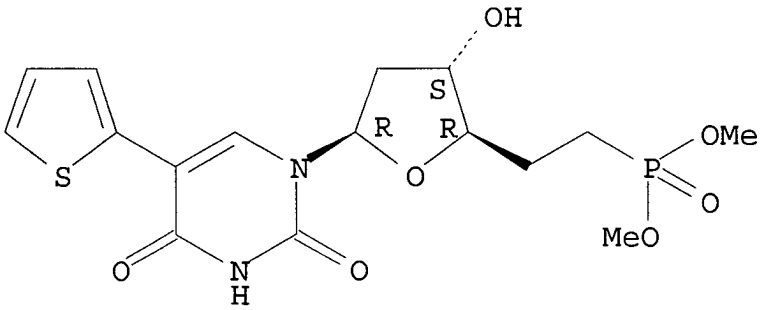
RN 127235-90-9 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-(2-thienyl)-1-[2,5,6-trideoxy-6-(dimethoxyphosphinyl)-.alpha.-D-erythro-hexofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 127235-91-0 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-(2-thienyl)-1-[2,5,6-trideoxy-6-(dimethoxyphosphinyl)-.beta.-D-erythro-hexofuranosyl]- (9CI) (CA INDEX NAME)

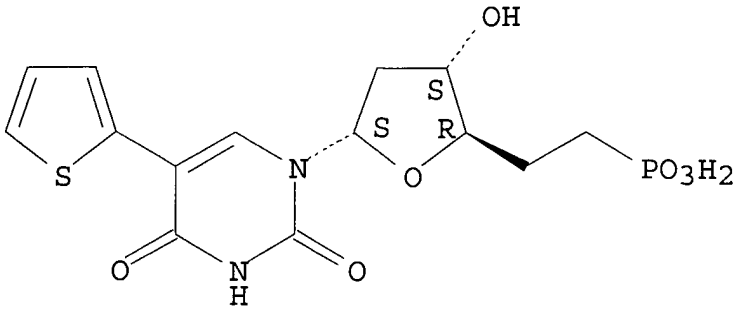
Absolute stereochemistry.



IT **127235-80-7P 127235-81-8P**
RL: BAC (Biological activity or effector, except adverse); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)
(prepn. of, as virucide)

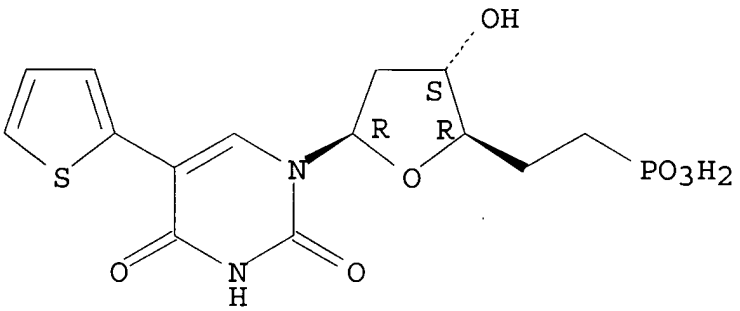
RN 127235-80-7 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-(2-thienyl)-1-(2,5,6-trideoxy-6-phosphono-.alpha.-D-erythro-hexofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



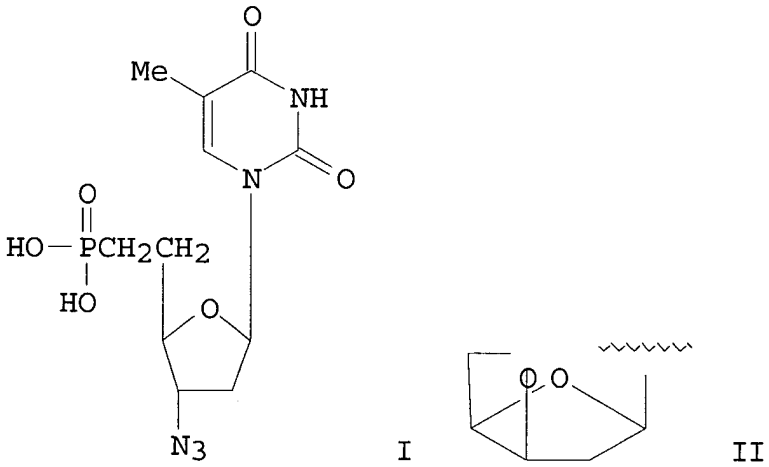
RN 127235-81-8 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-(2-thienyl)-1-(2,5,6-trideoxy-6-phosphono-.beta.-D-erythro-hexofuranosyl)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> D BIB ABS HITSTR 7

L28 ANSWER 7 OF 10 CAPLUS COPYRIGHT 1996 ACS
AN 1990:56529 CAPLUS
DN 112:56529
TI Cleavage of a nucleosidic oxetane with carbanions: synthesis of a highly promising candidate for anti-HIV agents. A phosphonate isostere of AZT 5'-phosphate
AU Tanaka, Hiromichi; Fukui, Mariko; Haraguchi, Kazuhiro; Masaki, Mariko; Miyasaka, Tadashi
CS Sch. Pharm. Sci., Showa Univ., Tokyo, 142, Japan
SO Tetrahedron Lett. (1989), 30(19), 2567-70
CODEN: TELEAY; ISSN: 0040-4039
DT Journal
LA English
OS CASREACT 112:56529
GI



I

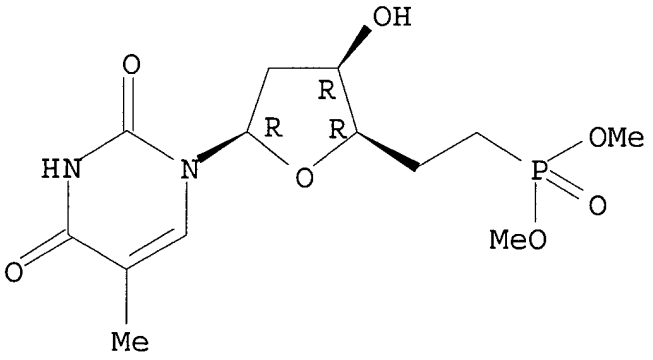
II

AB A phosphonate analog I of 3'-azido-3'-deoxythymidine (AZT) 5'-phosphate was synthesized via nucleophilic ring-opening of a nucleosidic oxetane II with (RO)2POCH2Li (R = Me, Et) as a key reaction step.

IT **124685-22-9P 124685-23-0P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)
(prepn. and mesylation of)

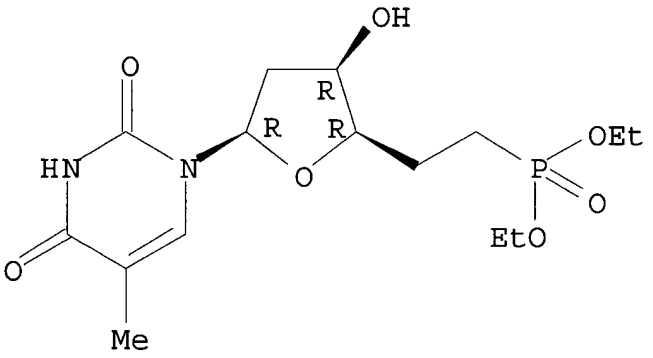
RN 124685-22-9 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-methyl-1-[2,5,6-trideoxy-6-(dimethoxyphosphinyl)-.beta.-D-threo-hexofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



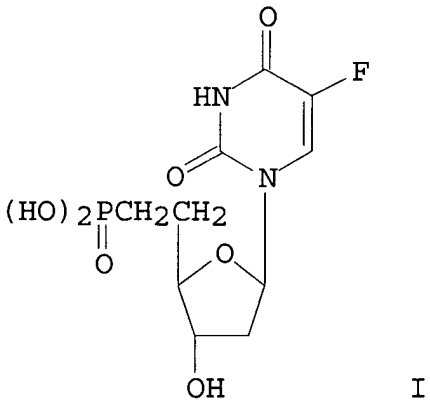
RN 124685-23-0 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-methyl-1-[2,5,6-trideoxy-6-(diethoxyphosphinyl)-.beta.-D-threo-hexofuranosyl]- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



=> D BIB ABS HITSTR 8

L28 ANSWER 8 OF 10 CAPLUS COPYRIGHT 1996 ACS
AN 1979:97373 CAPLUS
DN 90:97373
TI Phosphonate analog of 2'-deoxy-5-fluorouridylic acid
AU Montgomery, John A.; Thomas, H. Jeanette
CS Sch. Med., Tufts Univ., Boston, Mass., USA
SO J. Med. Chem. (1979), 22(1), 109-11
CODEN: JMCMAR; ISSN: 0022-2623
DT Journal
LA English
GI

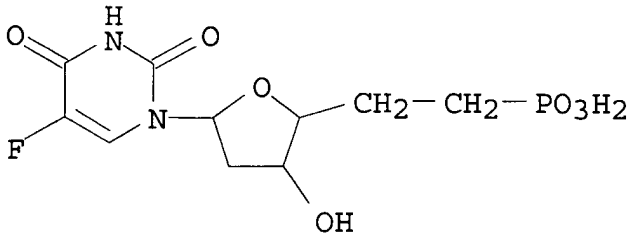


I

AB Ba 1-(2',5',6'-trideoxy-.beta.-D-ribohexofuranosyl)-5-fluorouracil-6'-phosphonate (I Ba) [**69124-08-9**] was prepd. by the oxidn. of 3'-O-acetyl-2'-deoxy-5-fluorouridine [2059-38-3] to the aldehyde, reaction of the aldehyde with diphenyl(triphenylphosphoranylidene)methylphosphonate [22400-41-5], to give the olefin, and redn. of the olefin to a satd. compd. followed by treatment with 3N NaOH. I inhibited thymidylate synthetase [9031-61-2] from Lactobacillus casei, Escherichia coli and Coliphage T2, and was cytotoxic to H. Ep-2 cells in culture.

IT **69124-08-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of and thymidylate synthetase inhibition by)

RN 69124-08-9 CAPLUS
CN 2,4(1H,3H)-Pyrimidinedione, 5-fluoro-1-(2,5,6-trideoxy-6-phosphono-.beta.-D-erythro-hexofuranosyl)-, barium salt (1:1) (9CI) (CA INDEX NAME)

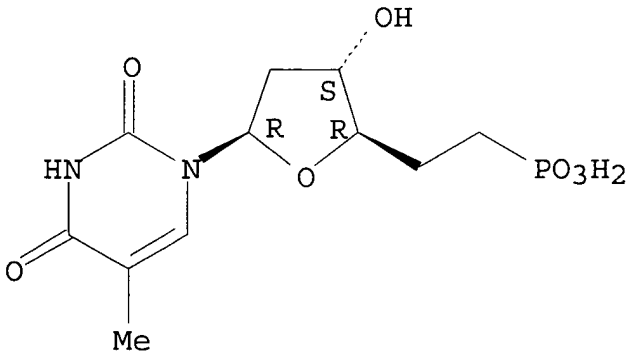


● 3/2 Ba

=> D BIB ABS HITSTR 9

L28 ANSWER 9 OF 10 CAPLUS COPYRIGHT 1996 ACS
AN 1971:530083 CAPLUS
DN 75:130083
TI Phosphorylated phosphonium ylids
PA Syntex Corp.
SO Brit., 22 pp.
CODEN: BRXXAA
PI GB 1243213 710818
PRAI US 670718 - 680229
DT Patent
LA English
AB The title compds. (I) are prepd. by condensing a monosubstituted phosphonium ylide with a phosphoryl halide in an inert solvent. I are converted into nucleoside 6'-phosphonates. Thus, 1.6M BuLi in hexane was added to methyltriphenylphosphonium bromide in ether at 20.degree.. After 0.5 hr, diphenyl phosphorochloridate in ether was slowly added and the product acidified and neutralized to give di-Ph triphenyl-phosphoranylidenemethylphosphonate (II). 2,3'-O-Anisylideneuridine-5'-carboxaldehyde was warmed 16 hr with II in THF to give di-Ph [1-(2,3-O-anisylidene-5,6-dideoxy-.beta.-D-ribo-hex-5-enofuranosyl)uracil] 6'-phosphonate.
IT **34393-67-4P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 34393-67-4 CAPLUS
CN Thymine, 1-(2,5,6-trideoxy-6-phosphono-.beta.-D-erythro-hexofuranosyl)- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



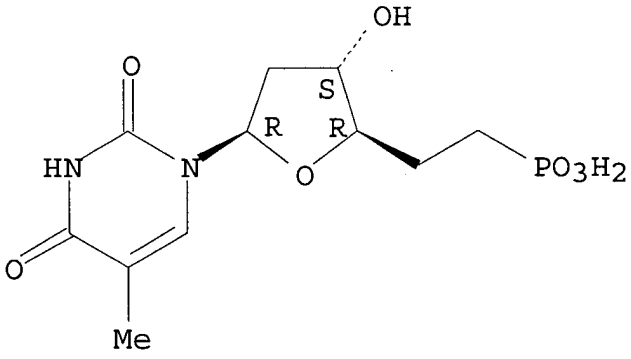
=> D BIB ABS HITSTR 10

L28 ANSWER 10 OF 10 CAPLUS COPYRIGHT 1996 ACS
AN 1971:518548 CAPLUS
DN 75:118548
TI Nucleoside 6'-phosphonic acids and the corresponding phosphonates
PA Syntex Corp.
SO Brit., 10 pp. Division of Brit. 1,243,213.
CODEN: BRXXAA
PI GB 1243214 710818
PRAI US 670718 - 680229
DT Patent
LA English
AB Nucleoside 5'-aldehyde are converted into nucleoside 6'-phosphonic acids by the treatment of the aldehydes with phosphorylated phosphonium ylides. Thus, 2',3-O-anisylideneuridine-5-aldehyde and Ph3P:CHP(O)(OPh)2 are kept 16 hr at 37.degree. in THF to give di-Ph [1-(2,3-O-anisylidene-5,6-dideoxy-.beta.-D-ribo-hex-5-enefuranosyl)uracil]-6' -phosphonate.
IT **34212-85-6P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(prepn. of)
RN 34212-85-6 CAPLUS
CN Thymine, 1-(2,5,6-trideoxy-6-phosphono-.beta.-D-erythro-hexofuranosyl)-, compd. with triethylamine (1:2) (8CI) (CA INDEX NAME)

CM 1

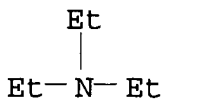
CRN 34393-67-4
CMF C11 H17 N2 O7 P
CDES 5:B-D-ERYTHRO

Absolute stereochemistry.



CM 2

CRN 121-44-8
CMF C6 H15 N



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=> D HIS L20-

     (FILE 'CAPLUS' ENTERED AT 08:33:14 ON 08 JUN 96)

     FILE 'REGISTRY' ENTERED AT 08:33:34 ON 08 JUN 96
L20           27 S L19 OR L17
L21            5 S L20 AND NCNC2-NCNC3/ES
L22            8 S L17 NOT L21
L23           15 S L19 NOT L21

     FILE 'CAPLUS' ENTERED AT 08:35:42 ON 08 JUN 96
L24            2 S L17
L25            1 S L21
L26           11 S L19
L27            1 S L24 NOT L25
L28           10 S L26 NOT L25

     FILE 'CAOLD' ENTERED AT 08:38:58 ON 08 JUN 96
L29            0 S L20

     FILE 'BEILSTEIN' ENTERED AT 08:39:50 ON 08 JUN 96
L30              STR L12
L31            1 S L11 AND L30
L32              STR L11
L33            1 SS L32 AND L30
L34            0 S L33 NOT L20
L35            6 SS L32 AND L30 FUL
L36            3 S L35 NOT L20

=>
```

=> D IDE RSD FA

L36 ANSWER 1 OF 3 COPYRIGHT 1996 Beilstein

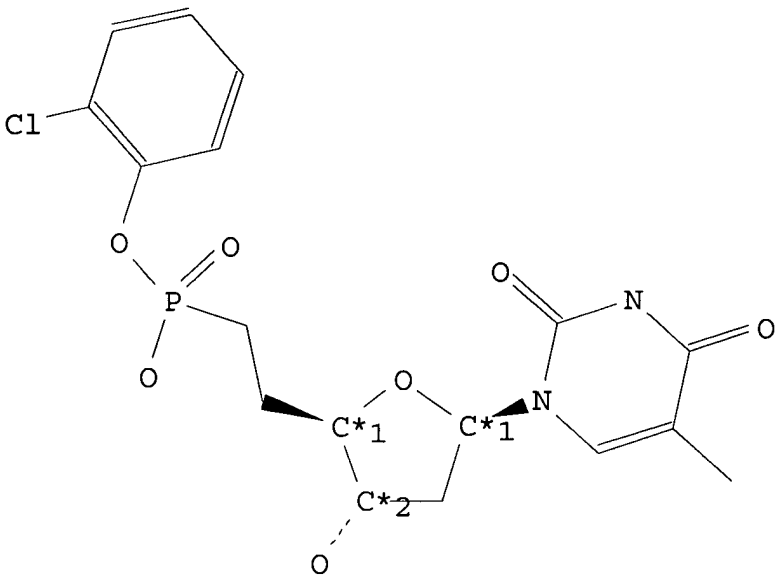
Beilstein Reg. No. (BRN): 7244822 Beilstein
Molecular Formula (MF): C17 H20 Cl N2 O7 P . C5 H5 N
Autonom Name (AUN): (2-<3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-tetrahydro-furan-2-yl>-ethyl)-phosphonic acid mono-(2-chloro-phenyl) ester; compound with pyridine
Beilstein Reference (SO): 6-24
General Comments (NTE): Stereo compound

Component Data:

Component Reg. No. (CBRN)	Component Molec. Formula (CMF)	Formula Weight (FW)	Lawson Number (LN)
7235314	C17 H20 Cl N2 O7 P	430.78	28796, 20810, 5220
103233	C5 H5 N	79.10	24225

CM 1

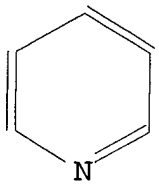
CBRN 7235314
CMF C17 H20 Cl N2 O7 P



Atom/Bond Notes:
1. CIP Descriptor: R
2. CIP Descriptor: S

CM 2

CBRN 103233
CMF C5 H5 N



Ring System Data:

Component BRN (CBRN): 7235314
Number of Rings (CNR): 3
Ring Systems (CNRS): 3
Diff. Ring Systems (CNDRS): 3
Ring Heteros (CNRH): 3
Acyclic Heteros (CNAH): 8

Beilstein Ring Index (BRIX)	Ring System Formula (RF)	BRIX Count
6.1.0-0.0-3.1	C6	1
5.1.0-1.2-0.0	C4O	1
6.1.0-2.3-1.2	C4N2	1

Component BRN (CBRN): 103233
Number of Rings (CNR): 1
Ring Systems (CNRS): 1
Diff. Ring Systems (CNDRS): 1
Ring Heteros (CNRH): 1

Beilstein Ring Index (BRIX)	Ring System Formula (RF)	BRIX Count
6.1.0-1.1-3.1	C5N	1

Field Availability:

Code	Name	Occur. (OCC)
MF	Molecular Formula	1
AUN	Autonom Name	1
FW	Formula Weight	2
SO	Beilstein Citation	1
LN	Lawson Number	4
NTE	Notes	1
SF	Stereo Family	1
PRE	Preparation	1
CTCPL	Coupling Phenomena	1
NMRA	NMR Absorption	3

=> D PRE

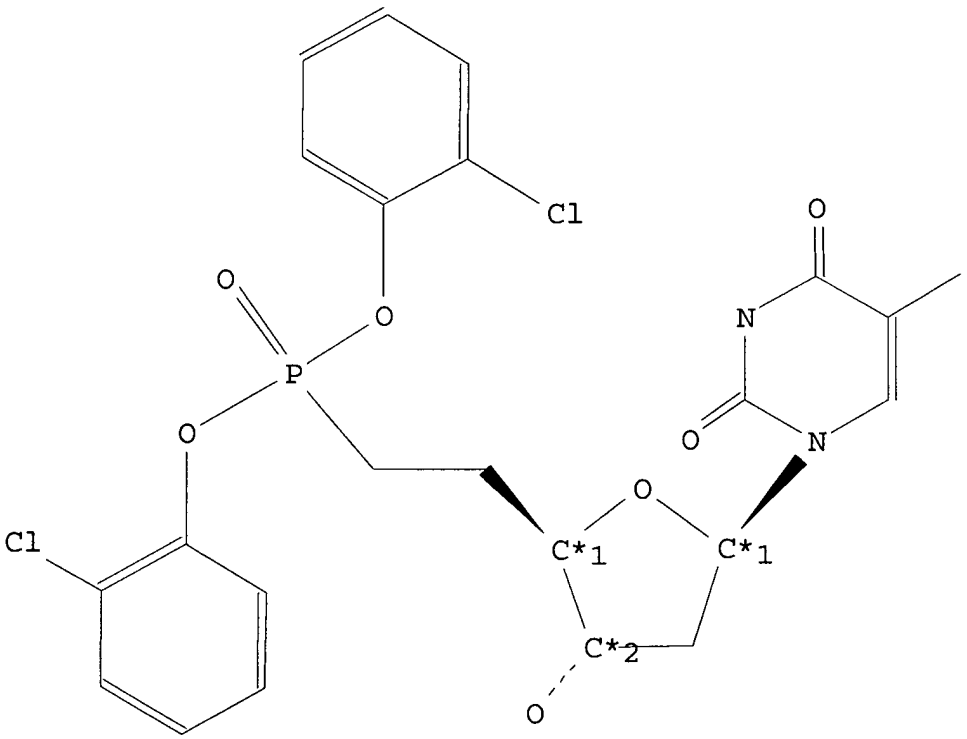
L36 ANSWER 1 OF 3 COPYRIGHT 1996 Beilstein

Preparation:
PRE
Start: BRN=7245684 2-chlorophenyl (3'-O-tert-butyldiphenylsilylthymidin-5'-yl)methylphosphonate triethylammonium salt, BRN=103233 pyridine
Reag: 1.) tetrabutylammonium fluoride trihydrate, 2.) Dowex 50W
Detail: 1.) THF, 4 h, 2.) water
Reference(s):
1. Szabo, Tomas; Stawinski, Jacek, Tetrahedron, 51 <1995> 14, 4145-4160, LA: EN, CODEN: TETRAB
Note(s):
2. Yield given. Multistep reaction

=> D IDE RSD FA 2

L36 ANSWER 2 OF 3 COPYRIGHT 1996 Beilstein

Beilstein Reg. No. (BRN):	6167605 Beilstein
Molecular Formula (MF):	C23 H23 Cl2 N2 O7 P
Autonom Name (AUN):	(2-<3-hydroxy-5-(5-methyl-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-tetrahydro-furan-2-yl>-ethyl)-phosphonic acid bis-(2-chloro-phenyl) ester
Beilstein Reference (SO):	6-24
General Comments (NTE):	Stereo compound
Formula Weight (FW):	541.32
Lawson Number (LN):	28796; 20810; 5220



Atom/Bond Notes:
1. CIP Descriptor: R
2. CIP Descriptor: S

Ring System Data:

Number of Rings (CNR):	4
Ring Systems (CNRS):	4
Diff. Ring Systems (CNDRS):	3
Ring Heteros (CNRH):	3
Acyclic Heteros (CNAH):	9

Beilstein Ring Index (BRIX)	Ring System Formula (RF)	BRIX Count
6.1.0-0.0-3.1	C6	2
5.1.0-1.2-0.0	C4O	1
6.1.0-2.3-1.2	C4N2	1

Field Availability:

Code	Name	Occur. (OCC)
MF	Molecular Formula	1
AUN	Autonom Name	1
FW	Formula Weight	1
SO	Beilstein Citation	1
LN	Lawson Number	3
NTE	Notes	1
SF	Stereo Family	1
PRE	Preparation	1
NMRA	NMR Absorption	1

=> D PRE 2

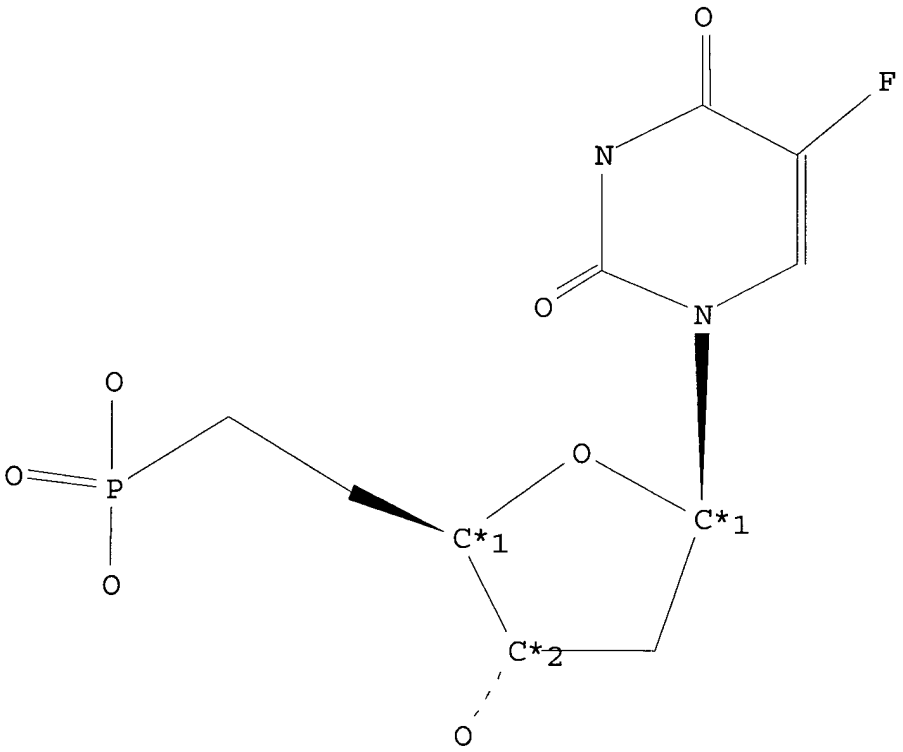
L36 ANSWER 2 OF 3 COPYRIGHT 1996 Beilstein

Preparation:
PRE
Start: BRN=6168856 C29H35Cl2N2O7PSi
Reag: H2, AcOH
Yield: 97.00 %
Solv: methanol
Catal.: Pd
Reference(s):
1. Boehringer, Markus P.; Graff, Darla; Caruthers, Marvin H., Tetrahedron Lett., 34 <1993> 17, 2723-2726, LA: EN, CODEN: TELEAY

=> D IDE RSD FA 3

L36 ANSWER 3 OF 3 COPYRIGHT 1996 Beilstein

Beilstein Reg. No. (BRN): 843003 Beilstein
Molecular Formula (MF): C10 H14 F N2 O7 P
Chemical Name (CN): (2-<5-(5-fluoro-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-2-hydroxy-tetrahydro-furan-2-yl>-ethyl)-phosphonic acid
Autonom Name (AUN): (2-<5-(5-fluoro-2,4-dioxo-3,4-dihydro-2H-pyrimidin-1-yl)-3-hydroxy-tetrahydro-furan-2-yl>-ethyl)-phosphonic acid
Beilstein Reference (SO): 5-24-06-00309
General Comments (NTE): Stereo compound
Formula Weight (FW): 324.20
Lawson Number (LN): 28795; 20810



Atom/Bond Notes:
1. CIP Descriptor: R
2. CIP Descriptor: S

Ring System Data:

Number of Rings (CNR): 2
Ring Systems (CNRS): 2
Diff. Ring Systems (CNDRS): 2
Ring Heteros (CNRH): 3
Acyclic Heteros (CNAH): 8

Beilstein Ring Index (BRIX)	Ring System Formula (RF)	BRIX Count
5.1.0-1.2-0.0	C4O	1
6.1.0-2.3-1.2	C4N2	1

Field Availability:

Code	Name	Occur. (OCC)
MF	Molecular Formula	1
CN	Chemical Name	1
AUN	Autonom Name	1
FW	Formula Weight	1
SO	Beilstein Citation	1
LN	Lawson Number	2
NTE	Notes	1
SF	Stereo Family	1
CDER	Chemical Derivative	1
CTUNCH	Unchecked Data	1

=> D CTUNCH CDER 3

L36 ANSWER 3 OF 3 COPYRIGHT 1996 Beilstein

CTUNCH Unchecked Data: Further information
Reference(s):
1. Montgomery et al., J.Med.Chem., 22 <1979>, 109, CODEN: JMCMAR

Chemical Derivative :
CDER 1,5 Ba, 1,5 H2O: aus Diphenylester 4, alk. Hydrolyse, BaOH; UV; NMR
Reference(s):
1. Montgomery et al., J.Med.Chem., 22 <1979>, 109, CODEN: JMCMAR

```
=> D HIS L37-

     (FILE 'MARPAT' ENTERED AT 08:45:43 ON 08 JUN 96)
L37            7 S L15 FUL
L38            7 S L30 SSS FUL SUB=L37

=> D QUE L38
L11             STR
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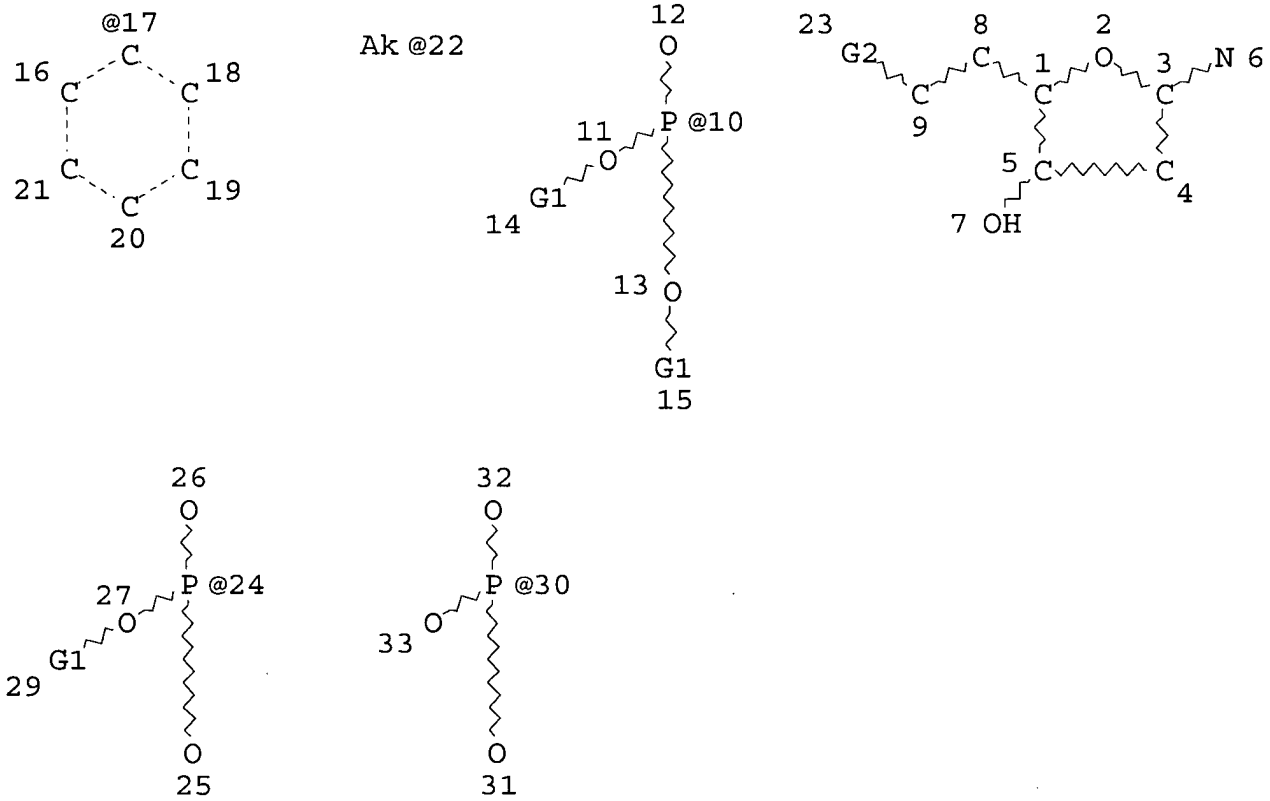
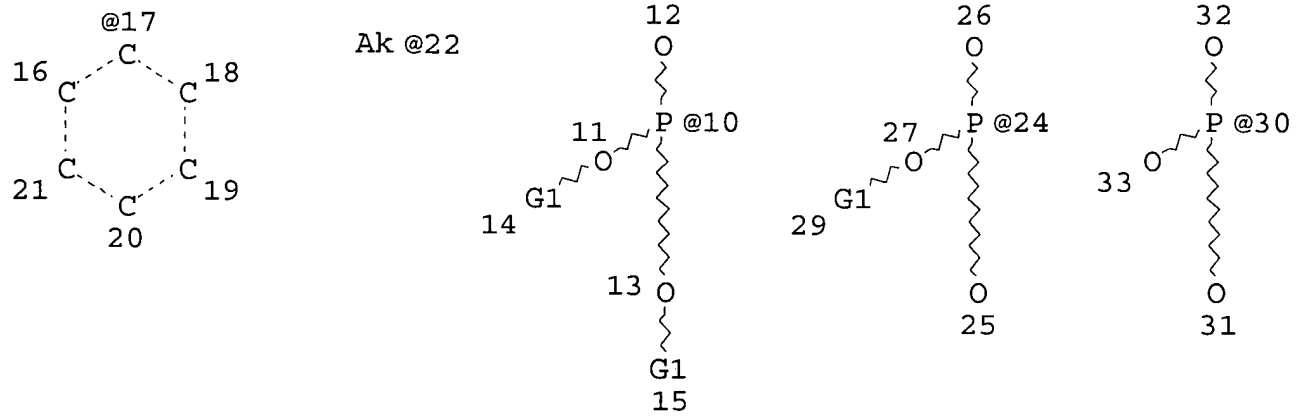
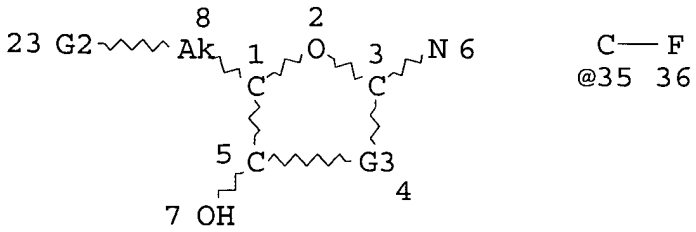



```
VAR G1=17/22
VAR G2=10/24/30
NODE ATTRIBUTES:
NSPEC    IS R       AT   6
CONNECT  IS E1  RC AT  12
CONNECT  IS E1  RC AT  22
CONNECT  IS E1  RC AT  25
CONNECT  IS E1  RC AT  26
CONNECT  IS E1  RC AT  31
CONNECT  IS E1  RC AT  32
CONNECT  IS E1  RC AT  33
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS  32

STEREO ATTRIBUTES: NONE
L30             STR
```





VAR G1=17/22
VAR G2=10/24/30
VAR G3=CH2/35
NODE ATTRIBUTES:
NSPEC IS R AT 6
CONNECT IS E2 RC AT 8
CONNECT IS E1 RC AT 12
CONNECT IS E1 RC AT 22
CONNECT IS E1 RC AT 25
CONNECT IS E1 RC AT 26
CONNECT IS E1 RC AT 31
CONNECT IS E1 RC AT 32
CONNECT IS E1 RC AT 33
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

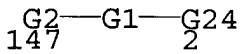
GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 33

STEREO ATTRIBUTES: NONE
L37 7 SEA FILE=MARPAT SSS FUL L11
L38 7 SEA FILE=MARPAT SUB=L37 SSS FUL L30

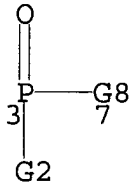
=> D QHIT BIB ABS

L38 ANSWER 1 OF 7 MARPAT COPYRIGHT 1996 ACS

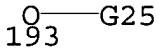
MSTR 1



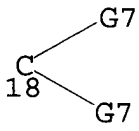
G1 = 7-2 3-147



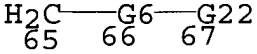
G2 = 193



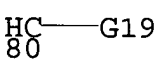
G6 = 18



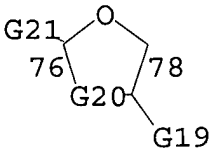
G8 = 65-3 67-2



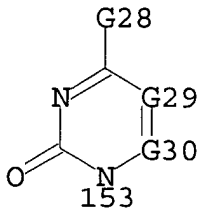
G19 = OH
G20 = 80



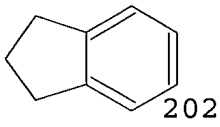
G22 = 76-66 78-2



G24 = 153



G25 = 202



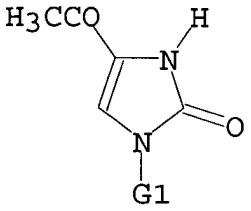
DER: or physiologically acceptable salts
MPL: claim 1
NTE: additional ring formation is allowed
NTE: substitution is restricted

AN 123:257269 MARPAT
TI Preparation of viricidal nucleotide analogs
IN Bischofberger, Norbert W.; Jones, Robert J.; Arimilli, Murty N.; Lin, Kuei-Ying; Louie, Michael S.; McGee, Lawrence R.; Prisbe, Ernest J.; Lee, William A.; Cundy, Kenneth C.
PA Gilead Sciences, Inc., USA
SO PCT Int. Appl., 154 pp.
CODEN: PIXXD2
PI WO 9507920 A1 950323
DS W: AM, AT, AU, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, ES, FI, GB, GE, HU, JP, KE, KG, KP, KR, KZ, LK, LT, LU, LV, MD, MG, MN, MW, NL, NO, NZ, PL, PT, RO, RU, SD, SE, SI, SK, TJ, TT, UA, US, UZ, VN
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG
AI WO 94-US10539 940916
PRAI US 93-123483 930917
US 94-193341 940208
DT Patent
LA English
GI For diagram(s), see printed CA Issue.
AB Nucleotide analogs [I; B = heterocyclic base; L1, L2 = amino acid or polypeptide residue; Z = (un)substituted 5-membered-ring-contg. (un)substituted hydrocarbyl residue; the dotted lines represent facultative bonds], useful as antiviral agents, antitumor agents (no data), and antineoplastic agents (no data), which are further characterized by the presence of an amidate-linked amino acid or an ester-linked group which is bonded to the P atom of phosphonate nucleotide analogs, are prepd. and their viricidal activity against HSV-1 and HSV-2 (strain 413-92) viruses presented. I comprise a phosphoamidate or ester bond that is hydrolyzed in vivo to yield a corresponding phosphonate nucleotide analog and methods and intermediates for I synthesis and use are also described.

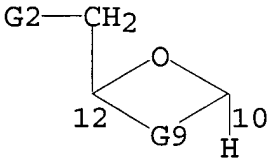
=> D QHIT BIB ABS 2

L38 ANSWER 2 OF 7 MARPAT COPYRIGHT 1996 ACS

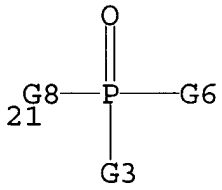
MSTR 1



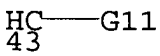
G1 = 10



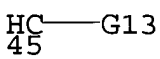
G2 = 21



G3 = OH
G6 = OH
G8 = CH2
G10 = 43



G11 = OH
G12 = 45



DER: or pharmaceutically acceptable salts
MPL: claim 2

AN 122:315045 MARPAT
TI Preparation of antiviral imidazolinone nucleoside derivatives.
IN Kalman, Thomas I.

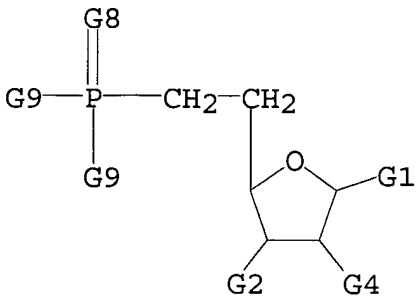
PA USA
SO PCT Int. Appl., 110 pp.
CODEN: PIXXD2
PI WO 9421658 A1 940929
DS W: CA, JP
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE
AI WO 93-US2472 930315
DT Patent
LA English
OS CASREACT 122:315045

AB Nucleoside or nucleotide analogs having a 4-acetylimidazolin-2-one base were prepd. Thus, 5-bromo-2'-deoxyuridine was refluxed 20 h in aq. NaHCO3, the reaction mixt. was passed through a column of Dowex 50W X8, and the resulting soln. of free acid was concd., dissolved in MeOH, and treated with CH2N2 to give Me 1-(2-deoxy-.beta.-D-ribofuranosyl)imidazolin-2-one-4-carboxylate. This was stirred with imidazole/tert-butyldimethylsilyl chloride in DMF to give Me 1-(2-deoxy-3,5-di-O-tert-butyldimethylsilyl-.beta.-D-ribofuranosyl)imidazolin-2-one-4-carboxylate, which was stirred with 1N NaOH in refluxing dioxane to give in DMF to give 1-(2-deoxy-3,5-di-O-tert-butyldimethylsilyl-.beta.-D-ribofuranosyl)imidazolin-2-one-4-carboxylic acid. This was stirred with Ac2O in pyridine to give a residue which was treated with MeLi in Et2O/PhMe to give 1-(2-deoxy-3,5-di-O-tert-butyldimethylsilyl-.beta.-D-ribofuranosyl)-4-acetylimidazolin-2-one. The latter was stirred with Dowex 50W X8 in MeOH/H2O to give 1-(2-deoxy-.beta.-D-ribofuranosyl)-4-acetylimidazolin-2-one. (dImd). DImd inhibited HIV-1 with EC50 = 8.1 .mu.M in MT-4 cells.

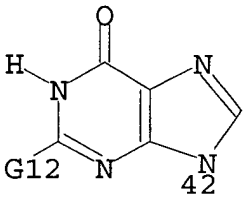
=> D QHIT BIB ABS 3

L38 ANSWER 3 OF 7 MARPAT COPYRIGHT 1996 ACS

MSTR 2

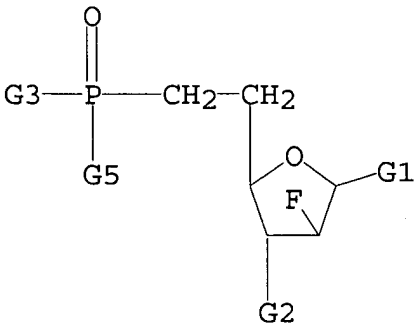


G1 = 42

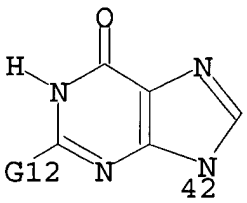


G2 = OH
G8 = O
G10 = O
G11 = Ph
DER: and tautomers
MPL: claim 9
STE: and stereoisomers

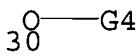
MSTR 4



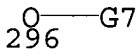
G1 = 42



G2 = OH
G3 = 30



G4 = Ph
G5 = 296



G7 = Ph
DER: and salts, zwitterions, and solvates
MPL: claim 38

AN 118:7326 MARPAT
TI Methylenephosphonate nucleoside analogs and oligonucleotide analogs made therefrom
IN Buhr, Chris; Matteucci, Mark; Bischofberger, Norbert W.; Froehler, Brian
PA Gilead Sciences, Inc., USA
SO PCT Int. Appl., 77 pp.
CODEN: PIXXD2
PI WO 9213869 A1 920820
DS W: AU, CA, FI, JP, KR, NO, RU
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, MC, NL, SE
AI WO 92-US1020 920207
PRAI US 91-652978 910208
DT Patent
LA English
GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Nucleoside phosphonates I [B = purine or pyrimidine nucleic acid base; R, R1 = (un)substituted OH, NH2, SH; R2 = H, allyloxy, allylthio, MeO, MeS, F; R3 = H, OH, F, OCH2Ph, OSiMe2CMe3, OCPh(C6H4OMe-4)2, OCPh2C6H4OMe-4; R2R3 = O, bond; X = O, S] were prepd. as intermediates for oligonucleotide analogs II (R4, R5 = H, protective group; n = 1-30). Thus, 3'-O-tert-butyldimethylsilyl-N2-isobutyryl-2'-deoxyguanosine was prepd. from 2'-deoxyguanosine in 3 steps and was treated with Ph3P:CHP(O)(OPh)2 followed by hydrogenation to give the phosphonate III.

=> D QHIT BIB ABS 4

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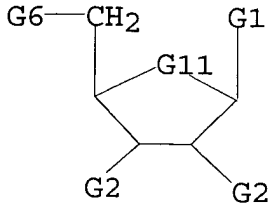
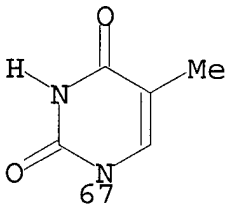
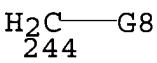
MSTR 1A



G1 = 67

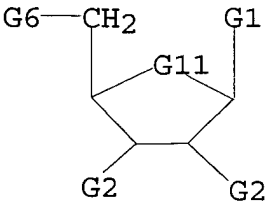


G2 = OH
G6 = 244

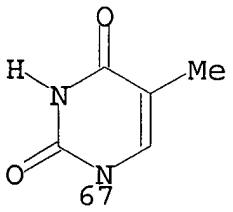


G8 = PO3H2
G11 = O
MPL: claim 1
NTE: also incorporates claim 3

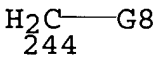
MSTR 1B



G1 = 67

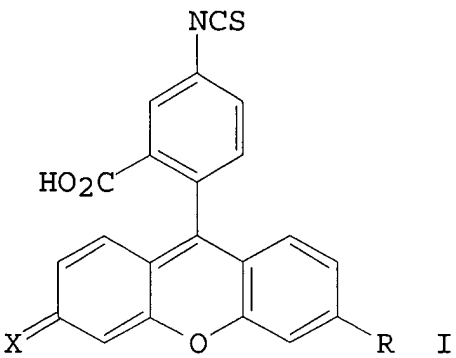


G2 = OH
G6 = 244

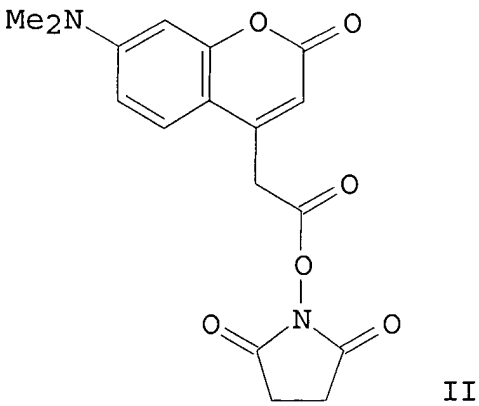


G8 = PO3H2
G11 = O
MPL: claim 1
NTE: also incorporates claim 3

AN 117:192263 MARPAT
TI 3'-/2'-Amino- or -thiol-modified, fluorescence coupled nucleoside and oligonucleotide, a method for their preparation and their use
IN Engels, Joachim; Herrlein, Mathias; Konrad, Renate; Mag, Matthias
PA Hoechst A.-G., Germany
SO Eur. Pat. Appl., 17 pp.
CODEN: EPXXDW
PI EP 490281 A1 920617
DS R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE
AI EP 91-120935 911206
PRAI DE 90-4039488 901211
DT Patent
LA German
OS CASREACT 117:192263
GI



I



II

AB The 2'- or 3'-hydroxy group of nucleosides, nucleotides, or

oligonucleotides were converted to an amino or thiol group then, coupled with fluorescent compds., eg. I (R = OH, X = O; R = Et2N, X = Et2N+; R = Me2N, X = Me2N+) and II. These modified oligonucleotides can be used for the synthesis of complements or of oligonucleotides for detection of generic material. The advantage of these nucleosides is the location of the fluorescent label; one does not have to introduce it during synthesis, as is done with current methods. Only a few polymerases used in synthesis can be inserted. The acceptance of the triphosphate by the polymerase decreases and a strong substrate excess is noted.

=> D QHIT BIB ABS 5

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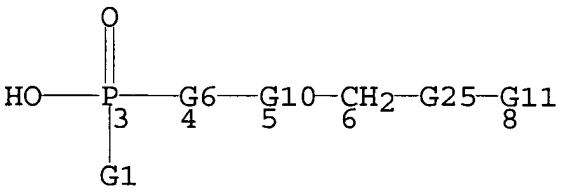
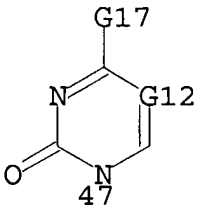
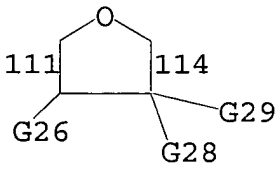
MSTR 1D



G1 = OH
G6 = alkylene<EC (1-4) C, DC (0) M3>
G11 = 47



G25 = 111-6 114-8



G26 = OH
DER: and pharmaceutically acceptable salts
MPL: claim 1
NTE: substitution is restricted
STE: and isomers

AN 117:111992 MARPAT
TI Phosphonate derivatives of certain nucleosides
IN Halazy, Serge; Casara, Patrick; Neises, Bernhard; Jund, Karin
PA Merrell Dow Pharmaceuticals, Inc., USA
SO Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
PI EP 477454 A1 920401
DS R: FR
AI EP 90-402695 900928
DT Patent
LA English
GI For diagram(s), see printed CA Issue.
AB Title phosphonates I [B = (un)substituted purinyl, pyrimidinyl, triazinyl, triazolyl, thiazolyl, selenazolyl; R = (un)substituted

alkyl; R1 = N3, F, Cl, OH, H; R2 = H, Cl, F, OH; R3 = H, Et; X = alkylene, oxaalkylene which may be unsatd. and/or substituted] and their 2',3'-didehydro analogs were prepd. for use as virucides, bactericides, and neoplasm inhibitors (no data). Thus, 3'-fluoro-2',3'-dideoxy-5-chlorouridine was treated with 2-bromoacetonyltetrahydropyran followed by CF3P(O)(OH)2 to give the phosphinate II.

=> D QHIT BIB ABS 6

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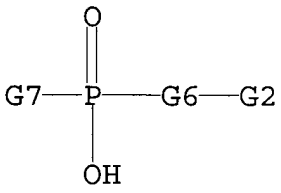
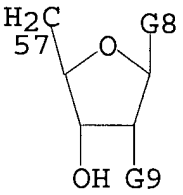
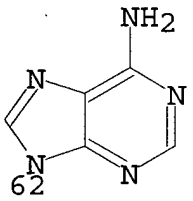
MSTR 3



G2 = 57



G6 = CH2
G7 = OH
G8 = 62



DER: and salts
MPL: claim 11

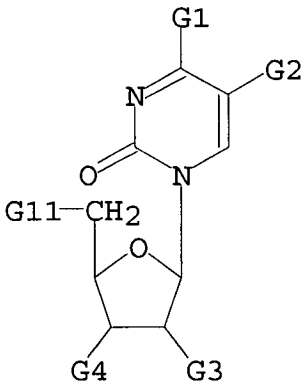
AN 116:152304 MARPAT
TI Synthesis of glycerol di- and triphosphate derivatives
IN Van den Bosch, Henk; Van Wijk, Bert; Kumar, Raj; Hostetler, Karl Y.
PA Vical, Inc., USA
SO PCT Int. Appl., 55 pp.
CODEN: PIXXD2
PI WO 9118914 A1 911212
DS W: AU, CA, JP
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE
AI WO 91-US3736 910529
PRAI US 90-530556 900529
DT Patent
LA English
AB Title compds. are prepd. by coupling RCH2CHR1CH2OP(O)(O-)L [R, R1 = OH, C1-24 alkyl with 0-6 sites of unsatn. (sic); L = leaving group] with a compd. having a terminal mono- or diphosphate group. Thus, dimyristoylphosphatidic acid morpholidate was heated with AZT

5'-monophosphate in pyridine to give 80% AZT dimyristoylglycerol diphosphate.

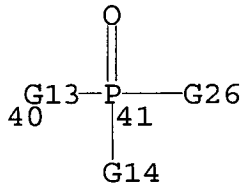
=> D QHIT BIB ABS 7

L38 ANSWER 7 OF 7 MARPAT COPYRIGHT 1996 ACS

MSTR 1A

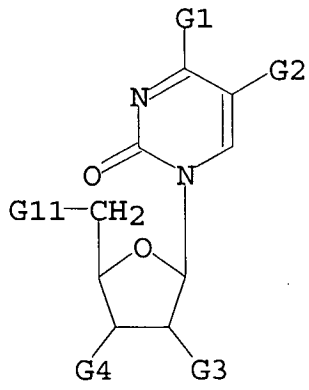


G4 = OH
G11 = 40

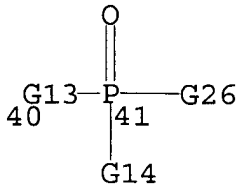


G14 = OH
G26 = OH
DER: and pharmaceutically acceptable salts
MPL: claim 1

MSTR 1B

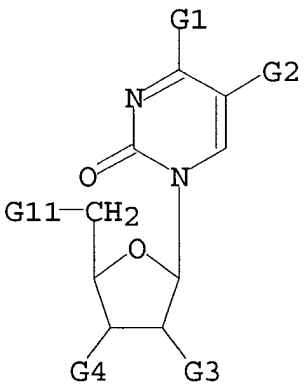


G4 = OH
G11 = 40

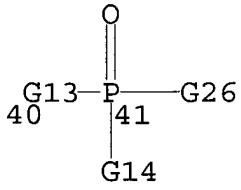


G14 = OH
G26 = OH
DER: and pharmaceutically acceptable salts
MPL: claim 1

MSTR 1C

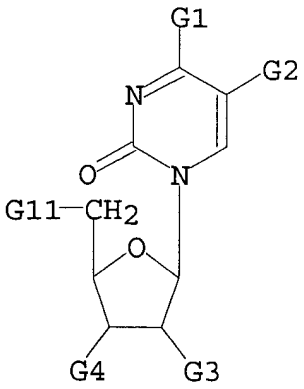


G4 = OH
G11 = 40

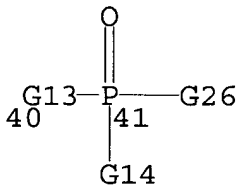


G14 = OH
G26 = OH
DER: and pharmaceutically acceptable salts
MPL: claim 1

MSTR 1D

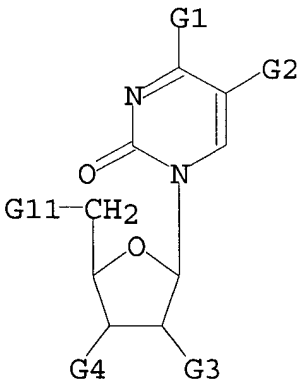


G4 = OH
G11 = 40

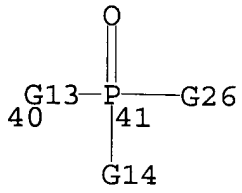


G14 = OH
G26 = OH
DER: and pharmaceutically acceptable salts
MPL: claim 1

MSTR 1E

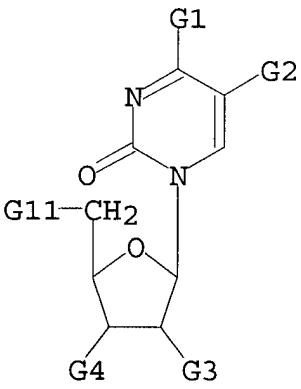


G4 = OH
G11 = 40

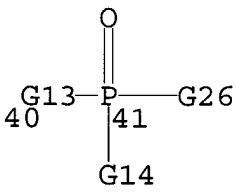


G14 = OH
G26 = OH
DER: and pharmaceutically acceptable salts
MPL: claim 1

MSTR 1F

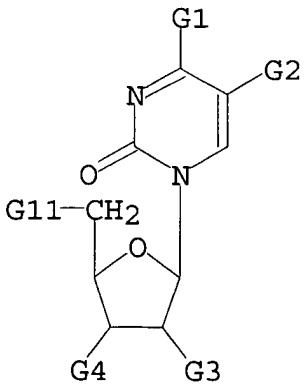


G4 = OH
G11 = 40

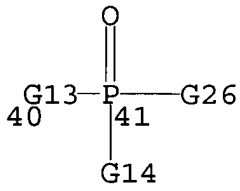


G14 = OH
G26 = OH
DER: and pharmaceutically acceptable salts
MPL: claim 1

MSTR 1G

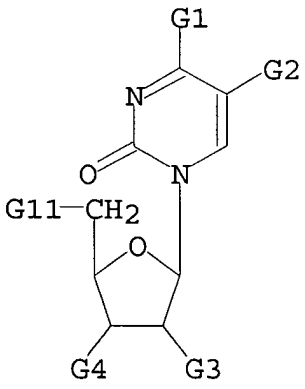


G4 = OH
G11 = 40

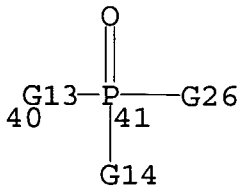


G14 = OH
G26 = OH
DER: and pharmaceutically acceptable salts
MPL: claim 1

MSTR 1H

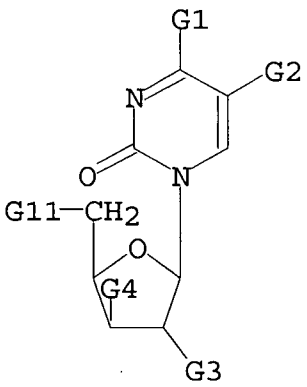


G4 = OH
G11 = 40

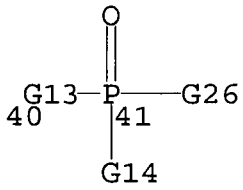


G14 = OH
G26 = OH
DER: and pharmaceutically acceptable salts
MPL: claim 1

MSTR 5A

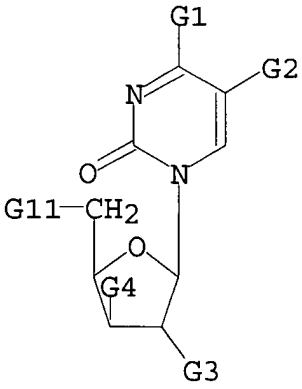


G4 = OH
G11 = 40

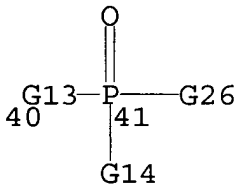


G14 = OH
G26 = OH
MPL: claim 23

MSTR 5B

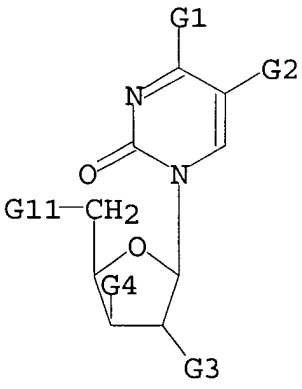


G4 = OH
G11 = 40

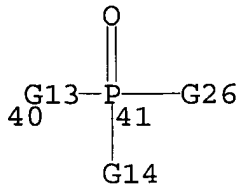


G14 = OH
G26 = OH
MPL: claim 23

MSTR 5C

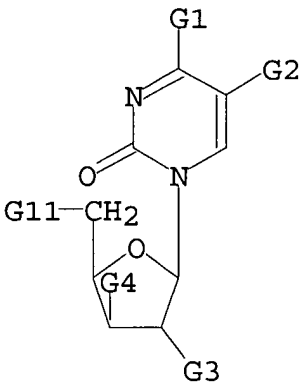


G4 = OH
G11 = 40

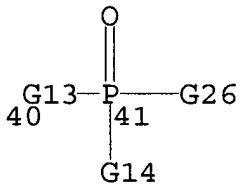


G14 = OH
G26 = OH
MPL: claim 23

MSTR 5D

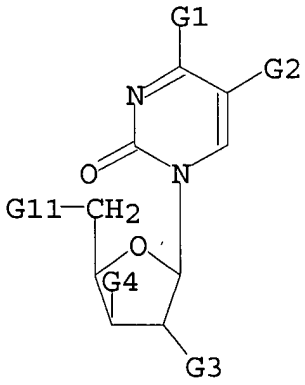


G4 = OH
G11 = 40

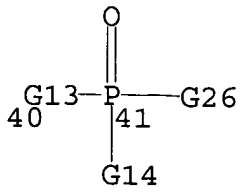


G14 = OH
G26 = OH
MPL: claim 23

MSTR 5E

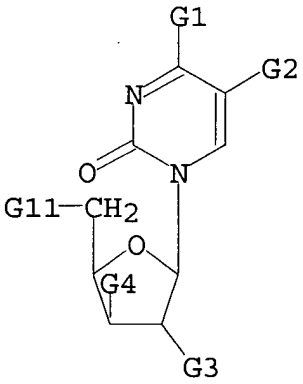


G4 = OH
G11 = 40



G14 = OH
G26 = OH
MPL: claim 23

MSTR 5F



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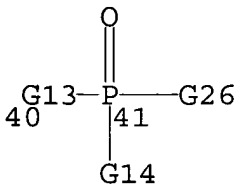
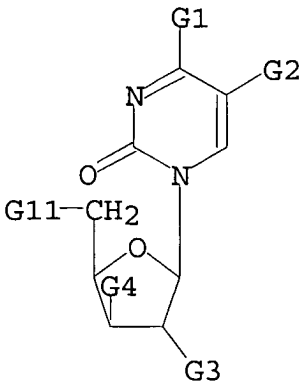
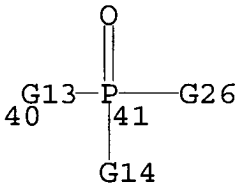


G14 = OH
G26 = OH
MPL: claim 23

MSTR 5G

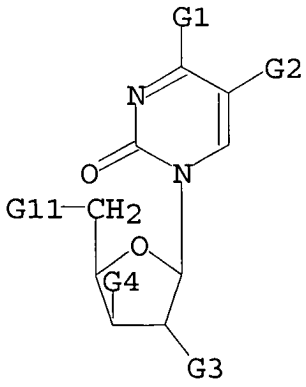


G4 = OH
G11 = 40

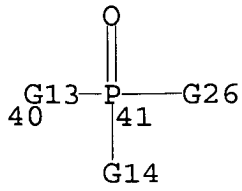


G14 = OH
G26 = OH
MPL: claim 23

MSTR 5H

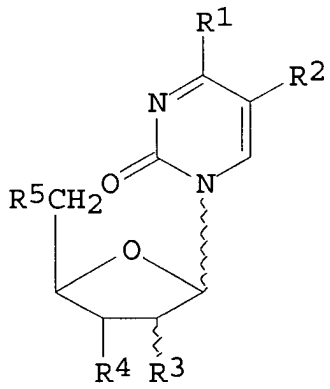


G4 = OH
G11 = 40



G14 = OH
G26 = OH
MPL: claim 23

AN 112:235778 MARPAT
TI Preparation of pyrimidine nucleosides as virucides and their intermediates
IN Johansson, K. Nils Gunnar; Malmberg, Hans C. G.; Noreen, Rolf; Sahlberg, S. Christer; Sohn, Daniel D.; Gronowitz, Salo
PA Medivir AB, Swed.
SO PCT Int. Appl., 57 pp.
CODEN: PIXXD2
PI WO 8912061 A1 891214
DS W: AU, DK, FI, HU, JP, KR, NO, US
AI WO 89-SE322 890607
PRAI SE 88-2173 880610
DT Patent
LA English
GI



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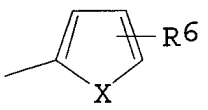
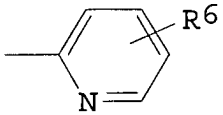
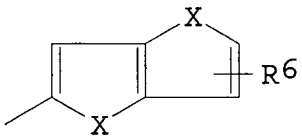
Q=  Q1=  Q2= 

AB The title compds. [I; R1 = OH, NH2; R2 = (hetero)aryl, e.g. Q-Q2; X = O, S, Se, (un)substituted NH; R3 = H, OH, F, OMe; R4 = H, F, OH or its ether or ester residue, OMe, cyano, C.tplbond.CH, N3; R5 = OH or its ether or ester residue, (CH2)nP(O)(OM)2, (CH2)nP(O)(OM)CH2P(O)(OM)2; R6 = H, straight or branched C1-10 alkyl, halo, etc.; M = H, a pharmaceutically acceptable counterion; n = 0, 1], useful for treatment of infections by viruses requiring reverse transcriptase for replication, e.g. human immunodeficiency virus (HIV) and hepatitis B virus, were prepd. Thus, silylation of 5-(2-thienyl)uracil (II) with hexamethyldisilazane in the presence of Me3SiCl and (NH4)2SO4 under reflux gave bis-trimethylsilylated II which was stirred overnight with 2-deoxy-3,5-di-O-p-toluoyl-D-ribofuranosyl chloride in ClCH2CH2Cl in the presence of mol. sieve 4A. The product was treated with MeONa in MeOH to give .alpha.- and

.beta.-I (R1 = R4 = R5 = OH, R2 = 2-thienyl, R3 = H). .alpha.-I in vitro showed IC50 of 0.05-10 .mu.M against HIV in H9 cells. Analogously prepd. and tested were addnl. 26 I. Cellular toxicity of I on H9 and F500 cells and inhibition of enzymes (e.g. HIV reverse transcriptase, hepatitis B virus DNA polymerase, and herpes simplex virus type 2 DNA polymerase) by I were also given.